REVIEWING FDA'S IMPLEMENTATION OF FDASIA

HEARING

BEFORE THE

SUBCOMMITTEE ON HEALTH

OF THE

COMMITTEE ON ENERGY AND COMMERCE

HOUSE OF REPRESENTATIVES

ONE HUNDRED THIRTEENTH CONGRESS

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C O N T E N T S

[1] Ms. Woodcock and Mr. Shuren submitted a joint statement for the record.
[2] Ms. Woodcock submitted a partial response to questions for the record.

REVIEWING FDA'S IMPLEMENTATION OF FDASIA

FRIDAY, NOVEMBER 15, 2013

HOUSE OF REPRESENTATIVES,
SUBCOMMITTEE ON HEALTH,
COMMITTEE ON ENERGY AND COMMERCE,
Washington, DC.

The subcommittee met, pursuant to call, at 10:02 a.m., in room 2322, Rayburn House Office Building, Hon. Joseph R. Pitts (chairman of the subcommittee) presiding.

Members present: Representatives Pitts, Burgess, Whitfield, Shimkus, Rogers, Murphy, Blackburn, Gingrey, Lance, Guthrie, Griffith, Bilirakis, Upton (ex officio), Pallone, Dingell, Engel, Capps, Green, Butterfield, Barrow, Castor, Sarbanes, and Waxman (ex officio).

Staff present: Clay Alspach, Chief Counsel, Health; Sean Bonyun, Communications Director; Noelle Clemente, Press Secretary; Brad Grantz, Policy Director, Oversight and Investigations; Sydne Harwick, Legislative Clerk; Robert Horne, Professional Staff Member, Health; Carly McWilliams, Professional Staff Member, Health; Andrew Powaleny, Deputy Press Secretary; Chris Sarley, Policy Coordinator, Environment and the Economy; John Stone, Counsel, Oversight; Ziky Ababiya, Democratic Staff Assistant; Eric Flamm, Democratic FDA Detailee; Karen Nelson, Democratic Deputy Committee Staff Director for Health; Rachel Sher, Democratic Senior Counsel; and Ryan Skukowski, Democratic Staff Assistant.

Mr. PITTS. The subcommittee will come to order. The Chair will recognize himself for an opening statement.

OPENING STATEMENT OF HON. JOSEPH R. PITTS, A REPRESENTATIVE IN CONGRESS FROM THE COMMONWEALTH OF PENNSYLVANIA

The Food and Drug Administration Safety and Innovation Act, FDASIA, was signed into law on July 9th, 2012. The purpose of the bill was to bring predictability, consistency, and transparency to FDA's regulation of drugs and devices. To that end, FDASIA reauthorized two successful user fee programs, the Prescription Drug User Fee Act, PDUFA, and the Medical Device User Fee Act, MDUFA, scheduled to expire at the end of fiscal year 2013. It also authorized two new user fee programs, for generic drugs, GDUFA, and biosimilars, BSUFA. In each case the industry negotiated a level of user fees to be paid to FDA in return for the agency meeting agreed-upon performance and accountability metrics.

Additionally, FDASIA permanently reauthorized the Best Pharmaceuticals for Children Act and the Pediatric Research Equity Act; reformed both the drug and medical device regulatory processes; addressed drug supply chain and drug shortage issues; and incentivized the development of new antibiotic drugs, among other provisions. The bill represents a bipartisan success not only for our committee, but for Congress as a whole. It passed the House by a voice vote and passed the Senate by a vote of 92–4.

Now, over a year later, we are here to examine whether the law has been a success for the American people, resulting in safer drugs and devices, faster approval times, and more consistency and predictability in the process. There is great congressional interest, not only in the overall implementation of FDASIA, but also in the day-to-day operational challenges and successes. And I would like to congratulate Dr. Woodcock for what I understand is significant progress in the Center for Drug Evaluation and Research.

I would like to welcome both Dr. Janet Woodcock and Dr. Jeffrey Shuren to the subcommittee. I look forward to hearing their testimony. And I yield 1 minute to Dr. Gingrey.

[The prepared statement of Mr. Pitts follows:]

PREPARED STATEMENT OF HON. JOSEPH R. PITTS

The subcommittee will come to order.

The Chair will recognize himself for an opening statement.

The Food and Drug Administration Safety and Innovation Act (FDASIA) was signed into law on July 9, 2012.

The purpose of the bill was to bring predictability, consistency, and transparency to FDA's regulation of drugs and devices.

To that end, FDASIA reauthorized two successful user fee programs, the Prescription Drug User Fee Act (PDUFA) and the Medical Device User Fee Act (MDUFA), scheduled to expire at the end of fiscal year 2013.

It also authorized two new user fee programs for generic drugs (GDUFA) and biosimilars (BSUFA).

In each case, industry negotiated a level of user fees to be paid to FDA in return for the Agency meeting agreed upon performance and accountability metrics.

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I would like to welcome both Dr. Janet Woodcock and Dr. Jeffrey Shuren to the subcommittee.

OPENING STATEMENT OF HON. PHIL GINGREY, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF GEORGIA

Mr. GINGREY. Mr. Chairman, thank you very much for yielding. I, too, am pleased to see Dr. Woodcock and Dr. Shuren again today. FDASIA looked to address the crisis of antibiotic resistance with

Title VIII, the GAIN Act, which I wrote with my colleagues Mr. Green, Mr. Shimkus, Ms. DeGette, Mr. Whitfield, and Ms. Eshoo.

By focusing on incentives to bring new drugs to market we have seen renewed focus on the development of cutting-edge drugs, antibiotic. However, even with the early success of this program, I do believe that we do need to do more.

And so, Mr. Chairman, CDC had a September report, CDC in my great capital center of Atlanta, Georgia, on antimicrobial resistance, highlights 18 known resistance threats. It is estimated that across the country more than 2 million people are sickened every year with antibiotic-resistance infections resulting in at least 23,000 deaths—23,000 deaths.

I look forward to continuing to work with the FDA to create innovative pathways and processes. We must make sure that the agency and drug developers have as many tools as possible to navigate this emerging public health problem.

And I yield back.

Mr. PITTS. The Chair thanks the gentleman.

And now yields the balance of time to Mr. Lance.

OPENING STATEMENT OF HON. LEONARD LANCE, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF NEW JERSEY

Mr. LANCE. Thank you, Mr. Chairman.

Today's hearing serves as a helpful pulse check of the FDA's implementation of the user fee agreements for the prescription drug, medical device, generic, and biosimilars industry signed into law last year. In New Jersey alone the life sciences support over 300,000 direct and indirect jobs and contributes more than $25 billion to the State's economy.

Historically the user fee agreements have improved the times of drug and devices, and today's hearing will help this committee gain further insight on how the FDA is carrying out these congressionally mandated responsibilities. It is important that regardless of the challenges the agency faces it remain committed to bringing innovative treatments to market and in the hands of patients who need them the most.

Thank you, Mr. Chairman. I look forward to hearing from our distinguished witnesses, Dr. Woodcock and Dr. Shuren, on these issues. And I yield back to you, sir.

Mr. PITTS. The Chair thanks the gentleman.

Now yields 5 minutes to the ranking member, Mr. Pallone, for an opening statement.

OPENING STATEMENT OF HON. FRANK PALLONE, JR., A REPRESENTATIVE IN CONGRESS FROM THE STATE OF NEW JERSEY

Mr. PALLONE. Thank you, Chairman Pitts.

And thank you to our witnesses for being here today. I am eager to hear your testimony about FDA's progress in implementing the Food and Drug Administration Safety and Innovation Act, or FDASIA.

Over 1 year ago, FDASIA was signed into law and, among other things, was designed to promote timely FDA review of drugs, med-

ical devices, generic drugs, and biosimilar biological products through the collection of user fees. It both renewed existing FDA user fee programs for pharmaceutical and medical device manufacturers and established new user fee programs for generic drugs and for lower cost versions of biotech drugs.

The user fees are an essential component of FDA's funding. They help to ensure a predictable and efficient review process so that the American public has access to safe and effective healthcare products.

For generics, at the time of enactment there was a backlog of over 2,500 applications for new generic drugs and a median review time of 31 months. These essential products typically cost 50 to 70 percent less than their brand name counterparts and have provided an estimated $1 trillion in savings to the Nation's healthcare system over the past decade. It is important that American consumers have access to these safe, effective, and low cost alternatives more quickly, which is why the provisions in the generic drug user fee agreement were so important, because it gave FDA the resources they need to make sure that happens. So I am interested to hear in that progress today.

FDASIA also gives FDA additional tools to ensure the safety of the global drug supply chain, such as requiring registration with the unique facility identifier for foreign and domestic drug establishments, administrative detention for adulterated or misbranded drugs, and increased penalties for counterfeit drugs. The additional authorities in FDASIA allow FDA to strengthen cooperation with foreign regulators as well.

These provisions were based on the ideas and proposals contained in the Drug Safety Enhancement Act, which I introduced with Mr. Dingell, Mr. Waxman, and Ms. DeGette. We worked hard with our Republican colleagues during consideration of this law to help FDA keep our medicines safer in this complex and ever-growing global supply chain.

We also included provisions in FDASIA to address drug shortages. FDASIA enhances early notification of supply interruptions for certain medically important drugs and directs FDA to establish a task force and submit a strategic plan on drug shortage mitigation, which FDA submitted to Congress last month. Early notification started as a result of an executive order in 2011 and was codified into law by FDASIA, and it has helped FDA to prevent shortages and to decrease the number of new shortages.

I will close by saying that FDASIA is the product of strong bipartisan collaboration and compromise that strengthens FDA's ability to safeguard the public health. What I outlined here today was only a snapshot of the promising provisions of the law. We strengthened both the agency and the public health by its passage while allowing companies to innovate in the process. And I am proud of the work we did in passing FDASIA, and I look forward to hearing about FDA's progress so far in implementing this law.

So I would like to yield the remainder of my time to Mr. Dingell.

OPENING STATEMENT OF HON. JOHN D. DINGELL, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF MICHIGAN

Mr. DINGELL. I thank my good friend for that.

This legislation is a fine example of the great work this committee can do when we put politics aside and work together in a bipartisan manner. I hope the committee will return to this spirit when considering a lot of other issues that will lie before us today and in following times.

One year ago, President Obama signed the Food and Drug Administration Safety and Innovation Act into law, the law [audio gap] user fee programs FAD. Big bold steps to improve supply chain safety, amongst other things. FDA now needs new innovative tools to deal with increasingly globalized supply chain [audio gap] succeed in their mission keeping the American people safe from harm from food, drugs, cosmetics, and other things.

I look forward to hearing from our witnesses today about the progress made by FDA and I commend you for having this hearing, and look forward to hearing from Food and Drug about what it is they are doing, how the matter is proceeding and how much more this committee must do to see to it that they are able to carry out their responsibilities.

Dr. Woodcock, welcome.

I yield back to my good friend Mr. Pallone the time that he so graciously yielded to me.

Mr. PALLONE. I yield back the balance of my time.

Mr. PITTS. The Chair thanks the gentleman.

Now recognize the chair of the full committee, Mr. Upton, 5 minutes for an opening statement.

OPENING STATEMENT OF HON. FRED UPTON, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF MICHIGAN

Mr. UPTON. Well, thank you again, Mr. Chairman. And I appreciate this morning's hearing on the implementation of the FDA Safety and Innovation Act.

You know, as many of us know, this was one of the committee's most significant bipartisan achievements in the last Congress, it really was. I particularly want to thank Dr. Woodcock, who is with us, and Dr. Shuren for coming today to provide an update on that implementation, something that we said we would do when it passed.

Last Congress this committee held at least 10 hearings on subjects related to the legislation, and at these hearings we focused on improving the predictability, consistency, and transparency of FDA's regulations of drugs and medical devices. Improving FDA regs is essential to fostering innovation which brings life-saving and life-improving drugs and medical devices to American patients and boosts job creation across the country, including southwest Michigan, most importantly.

I was very proud of the bipartisan work that we did in the last Congress, and I am pleased to hear that initial reports on implementation, especially at the Drug Center, are promising. Today is an opportunity to get an update on whether the FDA is meeting

its commitments related to the various user fees that we authorized, as well as the independent assessment of the device center.

It also is a chance to hear about how the FDA is implementing provisions related to rare diseases, drug shortages, an important provision that we wrote in, prescription drug abuse, and drug imports. These were provisions important to Republicans and Democrats, Americans across the country, and we look forward to working with the FDA on these issues. Our drug and device makers are global leaders in innovation and job growth, and we will continue working to ensure that they remain on top.

And I am prepared to yield to any of my Republican colleagues. Seeing none, I yield back the balance of my time.

[The prepared statement of Mr. Upton follows:]

PREPARED STATEMENT OF HON. FRED UPTON

Mr. Chairman, thank you for holding today's hearing on the implementation of the Food and Drug Administration Safety and Innovation Act. As many of you know, this was one of the committee's significant bipartisan achievements last Congress, and I thank Dr. Woodcock and Dr. Shuren for coming today to provide an update on implementation.

Last Congress, the committee held at least 10 hearings on subjects related to thelegislation. At these hearings, we focused on improving the predictability, consistency and transparency of FDA's regulation of drugs and medical devices. Improving FDA regulation is essential to fostering innovation, which brings lifesaving, life-improving drugs and medical devices to American patients and boosts job creation across the country, including southwest Michigan.

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Mr. PITTS. The Chair thanks the gentleman.

Now recognize the ranking member of the full committee, Mr. Waxman, 5 minutes for an opening statement.

OPENING STATEMENT OF HON. HENRY A. WAXMAN, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF CALIFORNIA

Mr. WAXMAN. Thank you, Mr. Chairman. I am pleased we are holding this oversight hearing on the legislation that we passed last year on a bipartisan basis, bipartisan, bicameral, and with the close working relationship with the Food and Drug Administration.

The bill had a number of important provisions. It reauthorized FDA's drug and medical device user fees programs, providing resources to enable the efficient review of applications and give patients access rapidly to new therapies. It reauthorized two pediatric programs which foster the development and safe use of prescription for children. Established two new user fee programs to help FDA speed up the review of new generics and biosimilars. It gave FDA new authorities to address a wide array of issues with respect to drugs and devices, new incentives for the development of anti-

biotics to treat serious and life-threatening infections. This was designed to ensure that the drugs we most need to protect us from dangerous resistant pathogens are the ones that are developed as quickly as possible.

This law also includes provisions to modernize FDA's authorities with respect to our increasingly globalized drug supply chain. Today 80 percent of the active ingredients in bulk chemicals used in U.S. drugs come from abroad and 40 percent of finished drugs are manufactured abroad. This law gave FDA new and improved tools to police today's dramatically different marketplace. The legislation addressed the crisis of drug shortages that has caused many problems for access to medicines in our country.

There are provisions relating to medical devices. I had some concerns about many of the device proposals, but we worked together to address these concerns with the goal of assuring that nothing in the House-passed bill took us backwards in terms of patient safety. And I hope Dr. Shuren will tell us today whether we succeeded in that goal or if there have been unintended and detrimental facts of this legislation.

Mr. Chairman, I thank you for holding this hearing. It is an important part of the job of Congress not just to work together to pass legislation, but to continue our review and oversight. I hope FDA will share with us whether there are any refinements or improvements to any of the law's provisions that we need to pass through the Congress. Our goal was and still is to ensure that the American public benefits from this legislation by getting access to safe and effective drugs and medical devices at the earliest possible time. I look forward to the testimony.

I do notice that I do have a couple of minutes left and if any member on our side of the aisle wants that time I would be happy to yield to them. And if not, I will offer the time to anybody on the other side of the aisle who wants to make any further comments. If not, I yield back the time.

Mr. PITTS. The gentleman yields back. Chair thanks the gentleman.

That concludes the opening statements.

On our panel today we have two witnesses from the U.S. Food and Drug Administration, Dr. Janet Woodcock, Director of the Center for Drug Evaluation and Research, and Dr. Jeffrey Shuren, Director of the Center for Devices and Radiological Health.

Thank you for coming. Your written testimony will be made a part of the record. We ask that you summarize your opening statements to 5 minutes. And at this time the Chair recognizes Dr. Woodcock for 5 minutes for an opening statement.

STATEMENTS OF JANET WOODCOCK, DIRECTOR, CENTER FOR DRUG EVALUATION AND RESEARCH, FOOD AND DRUG ADMINISTRATION; AND JEFFREY E. SHUREN, DIRECTOR, CENTER FOR DEVICES AND RADIOLOGICAL HEALTH, FOOD AND DRUG ADMINISTRATION

STATEMENT OF JANET WOODCOCK

Ms. WOODCOCK. Thank you and good morning. I am Janet Woodcock, head of the center for drugs at FDA.

The FDASIA legislation was really landmark legislation for drug regulation. It authorized two new user fee programs, one of which was critically needed to fix a problem, the problem of the backlog of generic drugs, a program that had become burdened by its own success and the massive filing of new generic drug applications that we had. And another one, which is more or less preventive, the biosimilars user fee program, hopefully will help us promptly review biosimilar drugs and get them on the market as we receive applications.

It also made two pediatric pieces of legislation permanent. And I am happy to say we passed a landmark of 500 labels that have been revised and updated with pediatric information because of this legislation. So 500 drug labels have information now for children that didn't before.

Additional pressing problems that were addressed included the lack of new pipeline for antibiotics, particularly for drug-resistant organisms, the drug shortage problem, and the supply chain safety issues. In addition, the legislation included a breakthrough designation program that has been very enthusiastically taken up, both by the industry and by the FDA, and many other provisions of course.

Congress laid out a very ambitious agenda and timeframe for our accomplishment of all of this, and we have been working hard, we have been very successful in implementing provisions. However, I brought our spreadsheet. This is two-sided, OK, tracking of all the obligations that we have under this legislation. And this isn't all of them, but it is certainly the ones that have hard deadlines. So we are trying to work against all these deadlines and make all of our timeframes and so forth.

I am happy to discuss this year's progress with you, and I look forward to working with the committee. Thank you.

Mr. PITTS. The Chair thanks the gentlelady.

Dr. Shuren, you are recognized 5 minutes for an opening statement.

STATEMENT OF JEFFREY E. SHUREN

Mr. SHUREN. Thank you. Mr. Chairman and members of the subcommittee, I am Dr. Jeff Shuren, Director, Center for Devices and Radiological Health, or CDRH, at the Food and Drug Administration.

FDASIA includes a third authorization of the Medical Device User Fee Act, or MDUFA III. Reauthorization of the medical device user fee program has helped to speed innovative new products to market without compromising safety and effectiveness. It did so by establishing new policies, procedures, and performance goals, and by boosting review capacity. It represents our commitment to increase the predictability, consistency, and clarity of our regulatory processes.

In exchange for the additional user fees, we work with stakeholders to develop much enhanced performance goals. We are committed to meeting those goals, and preliminary data indicates that we are on track to meet or exceed all of our fiscal year 2013 performance goals, and that includes a new shared goal with industry of average time to decision.

Since the early 2000s, CDRH's performance on several key measures had been steadily declining each year, reaching its lowest point in 2010. In 2010 we conducted an extensive assessment of our premarket programs, identified the problems, proposed solutions, sought extensive public input, and then issued a plan of action in January 2011, with some corrective action starting in 2010. Since 2010, due to the reforms we put in place in MDUFA III, we have seen improvement in these key measures. For example, our backlogs of 510(k) submissions and PMA applications are each down by about one-third. Our average total time to decision of PMA applications is down 37 percent. The percent of 510(k)s cleared and percent of PMAs approved are back up, in the case of PMAs back to where it was about a decade ago.

To provide greater transparency we are would providing substantially more detailed reporting on our progress in implementing performance goals. These reports are publicly available online and are discussed at quarterly meetings with industry.

FDASIA also includes provisions to streamline the de novo pathway for novel devices of low to moderate risk. Since passage of FDASIA, we have seen the number of de novo requests roughly double. We have also implemented process improvements and are seeing our review times for de novos trending downward as a result. As part of our MDUFA III commitments we agreed to implement our benefit-risk determination guidance we issued in March 2012. For the very first time and with public input we described the factors we would use in determining whether or not the benefits of the device outweigh its risk.

The framework we developed is flexible and patient-centric. For example, one factor we may take into account is patients' tolerance for risk and perspectives on benefits. Because patient viewpoints matter and to further implementation of the framework, earlier this year we launched our Patient Preferences Initiative. The initiative seeks to identify and validate tools for assessing patient preferences, establish an approach when incorporating those preferences into our device approval decisions, and then communicating that information publicly so that patients and practitioners can make better-informed decisions.

CDRH implemented the FDASIA provisions relating to investigational device exemptions, or IDEs. We have trained our staff and modified our decision letters to align them with FDASIA's requirement that FDA may not disapprove the clinical investigation on the basis that it would not support approving the device.

We have also taken several steps to facilitate first-in-human studies in the U.S. and to streamline our clinical trials program. As a result, the mean time for giving approval for manufactures to proceed with clinical studies of their devices has been cut almost in half.

We also recently announced a final rule for unique device identification, or UDI system, which will provide a standardized way to identify medical devices. The UDI reflects substantial input from the clinical community and from the device industry during all phases of its development. Once fully implemented the UDI system will provide improved visibility for devices as they move through the distribution change to the point of patient use, greatly enhanc-

ing our post-market surveillance capabilities and offering a way of documenting device use in electronic health records. We have also made good progress on classifying the remaining pre-amendment devices. Since passage of FDASIA we have issued 13 proposed orders.

Implementing the device-related provisions of FDASIA is a massive undertaking, but we are committed to doing it in a way that provides lasting improvement to public health. Mr. Chairman, I commend the subcommittee's efforts and am pleased to answer any questions.

[The prepared statement of Ms. Woodcock and Mr. Shuren follows:]

DEPARTMENT OF HEALTH AND HUMAN SERVICES Public Health Service

Food and Drug Administration
Silver Spring, MD 20993

STATEMENT

OF

JANET WOODCOCK, M.D.

DIRECTOR
CENTER FOR DRUG EVALUATION AND RESEARCH

AND

JEFFREY SHUREN, M.D., J.D.

DIRECTOR
CENTER FOR DEVICES AND RADIOLOGICAL HEALTH

FOOD AND DRUG ADMINISTRATION

DEPARTMENT OF HEALTH AND HUMAN SERVICES

BEFORE THE

SUBCOMMITTEE ON HEALTH
COMMITTEE ON ENERGY AND COMMERCE

U.S. HOUSE OF REPRESENTATIVES

"REVIEWING FDA'S IMPLEMENTATION OF FDASIA"

November 15, 2013

RELEASE ONLY UPON DELIVERY

INTRODUCTION

Mr. Chairman and Members of the Subcommittee, we are Dr. Janet Woodcock, Director of the Center for Drug Evaluation and Research (CDER) and Dr. Jeffrey Shuren, Director of the Center for Devices and Radiological Health (CDRH), at the Food and Drug Administration (FDA or the Agency), which is part of the Department of Health and Human Services (HHS). Thank you for the opportunity to be here today to discuss implementation of the Food and Drug Administration Safety and Innovation Act (FDASIA) (P.L. 112-144). We appreciate the extensive bipartisan efforts of this Subcommittee in crafting the legislation and passing it well in advance of the statutory deadline for user fee reauthorization.

On July 9, 2012, President Obama signed FDASIA into law, reauthorizing user fee programs for innovator drugs and medical devices and establishing two new user fee programs for generic drugs and biosimilar biological products. The law also gave FDA new authority to better protect the drug supply chain, which is critical in an increasingly global marketplace. In addition, FDASIA provided the Agency with new authorities to combat drug shortages and stimulate antibacterial drug development, made permanent programs to enhance development of products used to treat pediatric populations, included provisions intended to encourage drug innovation, made a number of important changes to medical device regulation, and added a number of other important provisions. As we discuss below, FDA has made significant progress in implementing FDASIA and is on track to meet most due dates. We have established a three-year implementation plan, which we have been updating monthly to keep the public informed.

User Fee Program Implementation

FDASIA includes the fifth authorization of the Prescription Drug User Fee Act (PDUFA V), which was first enacted in 1992, and the third authorization of the Medical Device User

Fee Act (MDUFA III), which was first enacted in 2002. Two new user fee programs—for generic drugs and for biosimilar biological products—build on the successes of these two established user fee programs. Coming at a time of continuing budget restraints, this steady source of funding is essential to support and maintain FDA's staff of experts who review the thousands of product submissions we receive every year, and do so in a timely and thoughtful manner. Over the years, our user fee programs have ensured predictable, consistent, and streamlined premarket programs for industry and have helped speed patient access to safe and effective new products. It is important to note that, due to across-the-board budget cuts imposed by sequestration, approximately $56 million in FY 2013 user fee funds from PDUFA, MDUFA, the Generic Drug User Fee Amendments (GDUFA), and the Biosimilar User Fee Act (BsUFA) are unavailable to FDA, which puts at risk key commitments negotiated under FDASIA. For example, the reductions in PDUFA and MDUFA funds may result in delays in the availability of novel and important new drugs and devices for patients. Sequestration also poses a challenge for FDA as we take the necessary steps to launch the new user fee programs for generic drugs and biosimilars. These programs are designed to enable FDA to leverage user fee resources to provide many benefits to the public, including expediting the availability of high-quality, cost-effective generic drugs and biosimilars.

PDUFA

PDUFA V addressed many of the top priorities identified by public stakeholders, the top concerns identified by industry, and the most important challenges identified within FDA. PDUFA V enhancements included increased interaction during regulatory review of New Molecular Entity New Drug Applications (NME NDAs) and original Biologics License Applications (BLAs); regulatory science enhancements to expedite drug development; the development of important new guidance for drug developers; a commitment to develop a

structured framework for benefit-risk assessment; various enhancements to the drug safety system; and requirements for electronic submissions and standardization of electronic application data. This additional work was funded by a modest 6 percent increase in PDUFA user fees. In fiscal year 2013, however, the amount sequestered from PDUFA fees nearly cancelled out the 6 percent increase in fee funding.

GDUFA

One of FDA's major undertakings since last July has been putting in place the infrastructure for a new generic drug user fee program that will expedite the availability of low-cost, high-quality generic drugs. The program has already achieved several milestones, including making significant strides in reducing the backlog of pre-GDUFA applications and enhancing review efficiencies. FDA has completed scientific review of approximately 40 percent of GDUFA backlog applications since the program launch. In addition, FDA has conducted completeness assessments for over 900 drug master files[1] and has launched the creation of a public list of drug master files available for reference to expedite review of applications containing referenced active pharmaceutical ingredients (API). Further, FDA held a public meeting on June 21, 2013, to discuss regulatory science priorities to expand the availability and quality of generic drugs and solicit input from stakeholders. The Agency streamlined the hiring process to recruit new scientific reviewers, project managers, investigators, and support staff, and met its ambitious year-one GDUFA hiring goal by bringing on board at least 25 percent of GDUFA program hires by October 1. Lastly, FDA has facilitated development of the most comprehensive list of generic drug industry participants: as of October 1, 2013, more than 2,200 manufacturing and testing facilities have submitted self-identification information to FDA, enhancing the quality and transparency of our knowledge of the generics industry.

[1] Drug Master Files are widely used to provide FDA with information about the drug substance, also known as the API.

MDUFA

Reauthorization of the medical device user fee program has helped to expedite the availability of innovative new products to market by boosting the medical devices regulatory review capacity through hiring new staff. MDUFA III represented a commitment between the U.S. medical device industry and FDA to increase the efficiency of regulatory processes in order to reduce the total time it takes to make decisions on safe and effective medical devices. It was the result of more than a year of public input, negotiations with industry representatives, and discussions with patient and consumer representatives.

As we have previously testified, prior to MDUFA III, beginning in 2010, we put in place a series of reforms designed to improve predictability, consistency, and clarity in the device review process.[2] We were seeing results from these reforms before enactment of MDUFA III, but the additional user fee funding authorized under FDASIA enhances our ability to implement positive changes for patients and industry. Under MDUFA III, FDA is authorized to collect user fees that will total approximately $595 million over five years. With this additional funding, plus stable appropriated funding, FDA intends to hire more than 200 full-time equivalent (FTE) workers over the course of MDUFA III. As of October 1, 2013, we have hired more than 90 new employees in support of the medical device review process.

In exchange for the additional user fees, FDA committed to meet much-enhanced performance goals for the device review process. Preliminary data indicate that FDA has the potential to meet all of its FY 2013 MDUFA III performance goals and expects to see a 25 percent decrease in the

[2] See CDRH, "Medical Device Pre-Market Programs: An Overview of FDA Actions" (Oct. 19, 2011) and "Accomplishments: CDRH Plan of Action for 510(k) and Science" (February 2013), available at *http://www.fda.gov/aboutfda/centersoffices/officeofmedicalproductsandtobacco/cdrh/cdrhreports/ucm239448.htm.*

backlog of 510(k) submissions. In addition, FDA expects to see a decrease in average total time for review of 510(k) submissions and Premarket Approval (PMA) Applications.

FDA is providing substantially more detailed quarterly reporting on our progress in implementing those performance goals, and our quarterly performance reports are online and available to the public. These reports are also presented and discussed at FDA-conducted, quarterly meetings with representatives from medical device member organizations.

In addition, FDA and the medical device industry agreed in MDUFA III to have an independent contractor conduct a two-phase assessment for performing technical analysis, a management assessment, and program evaluation required to objectively assess FDA's premarket review processes. This assessment is currently in process. High-priority findings are expected to be published by the end of this calendar year.

BsUFA

The Biologics Price Competition and Innovation Act (BPCI Act), which was enacted as part of the Affordable Care Act, established a new abbreviated approval pathway for biological products shown to be "biosimilar to" or "interchangeable with" an FDA-licensed biological product. Approved biosimilars are expected to be less expensive than the reference products, providing clinicians and their patients access to more affordable treatments that are biosimilar or interchangeable.

BsUFA addresses many of the top priorities identified by public and industry stakeholders and the most important challenges identified by FDA in bringing biosimilar products to market. The biosimilars user fee program is similar to the PDUFA program in that it includes fees associated

with marketing applications, manufacturing establishments, and products. However, there are some differences between BsUFA and PDUFA because of the nascent state of the biosimilars industry in the United States. For example, there are currently no FDA-approved biosimilar biological products; accordingly, the biosimilars user fee program includes fees for products that are in the development phase to generate fee revenue in the near-term and to enable sponsors to have meetings with FDA early in the development of biosimilar biological product candidates.

In March 2013, FDA published a draft guidance for industry entitled "Formal Meetings Between the FDA and Biosimilar Biological Product Sponsors or Applicants."[3] This draft guidance provides recommendations to industry on formal meetings between FDA and sponsors or applicants relating to the development and review of biosimilar biological products regulated by the Center for Drug Evaluation and Research (CDER) and the Center for Biologics Evaluation and Research (CBER). The guidance assists sponsors and applicants in generating and submitting a meeting request and the associated meeting package to FDA for biosimilar biological products.

As of September 17, 2013, FDA had received 56 meeting requests for an initial meeting to discuss biosimilar development programs related to 13 different reference products and had held 47 initial meetings with sponsors. FDA is actively engaging with sponsors, including holding development-phase meetings and providing written advice for ongoing development programs for proposed biosimilar products. As of September 17, 2013, CDER had received 17 Investigational New Drug (IND) Applications for biosimilar development programs, although additional development programs are proceeding under pre-INDs.

[3] *http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm345649.pdf.*

Implementation of the Additional FDASIA Provisions

User fees are by no means the only focus of the law. FDASIA also includes provisions to strengthen the drug supply chain; enhance patient engagement with FDA; address the problem of drug shortages; promote innovation; promote the development of antibacterial drugs; encourage the development of drugs and devices for use in pediatric populations; and enhance FDA's medical device premarket review program, among others.

Global Drug Supply Chain

Title VII of FDASIA strengthens drug safety by giving FDA new authorities to protect the integrity of an increasingly global drug supply chain in which nearly 40 percent of finished drugs and 80 percent of APIs are imported. Title VII allows FDA to protect the global drug supply chain by: (1) increasing FDA's ability to collect and analyze data to enable risk-informed decision-making, (2) advancing risk-based approaches to facility inspection, (3) partnering with foreign regulatory authorities, and (4) driving safety and quality throughout the supply chain through strengthened enforcement tools.

Since enactment of FDASIA, FDA has been working diligently to implement the Title VII supply chain authorities in a meaningful way that strives to maximize its public health impact. For example, FDA issued a proposed rule to extend the Agency's administrative detention authority to include drugs intended for human or animal use, in addition to the authority that is already in place for foods, tobacco, and devices; issued draft guidance defining conduct that the Agency considers delaying, denying, limiting, or refusing inspection, resulting in a drug being deemed adulterated; issued draft guidance addressing specification of the unique facility identifier system for drug establishment registration; and successfully worked with the U.S. Sentencing Commission on higher penalties relating to adulterated and counterfeit drugs.

The Agency had already taken steps toward development of a risk-based inspection schedule, prior to FDASIA. However, the enhancements provided by FDASIA will further assist the Agency in responding to the complexities of an increasingly globalized supply chain. For example, provisions in FDASIA that permit FDA to request records in advance or in lieu of an inspection and that require firms to submit a unique facility identifier will allow FDA to increase its inspectional efficiency and its knowledge base.

In addition, FDA hosted a public meeting in July 2013 to solicit comments from the public about implementation of Title VII generally, and to specifically address the provisions related to standards for admission of imported drugs and commercial drug importers, including registration requirements and good importer practices.

Title VII implementation requires not only the development of new regulations, guidance, and reports, but also major changes in FDA information systems, processes and policy—a challenging task given that Title VII was not additionally funded through user fee support or otherwise. However, FDA has worked to make progress in each of these areas, prioritizing the Agency's efforts to achieve the greatest public health impact and deploy its limited resources most effectively.

Patient Engagement

In accordance with our commitments in PDUFA V, FDA has initiated the Patient-Focused Drug Development Program. The objective of this five-year effort is to more systematically obtain the patient's perspective on a disease and its impact on patients' daily lives, the types of treatment

benefit that matter most to patients, and the adequacy of the available therapies for the disease. We have already held patient meetings on several major diseases.

CDRH launched a comprehensive Patient Preference Initiative earlier this year. This Initiative builds upon our 2012 Benefit-Risk Guidance entitled "Factors to Consider When Making Benefit-Risk Determinations in Medical Device Premarket Approval and De Novo Classifications,"[4] which outlines the principal factors FDA considers when making benefit-risk determinations during the premarket review process for certain medical devices, including patient perspectives on meaningful benefits and acceptable risks. However, while this guidance outlines a strategy for how patient preference results should be compared to other sections of a submission, it does not outline which methods, tools, and approaches can be used to collect patient views or provide guidance on how to establish and evaluate the validity of the data, nor does it describe how patient preference data may be used in a broader context of the total product cycle of medical devices.

Therefore, CDRH established the Patient Preference Initiative to provide the information, guidance, and framework necessary to incorporate patient preferences on the benefit-risk tradeoffs of medical devices into the full spectrum of CDRH regulatory processes and to inform medical device innovation by the larger medical device community. CDRH held a two-day public workshop in September 2013 to engage and solicit information on patient preference from stakeholders, including patients, providers, industry, and academic thought leaders. CDRH has also recently completed an obesity pilot study that has developed new tools that can be used to measure patient preferences. Finally, CDRH is working to expand both the number of patient Special Government Employees (SGEs) and the ways in which FDA uses these expert patients throughout the Agency.

[4] *http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM296379.pdf.*

Drug Shortages

Preventing drug shortages is, and will continue to be, a priority for FDA. Our performance in this area has improved over the past two years, including in response to the President's Executive Order in 2011 and the passage of FDASIA. In 2012, there were 117 new drug shortages, a decrease of more than 50 percent from the previous year. Overall, significant progress is being made to prevent and mitigate drug shortages as a result of collaboration between FDA, industry, and other stakeholders. FDA has worked hard to prevent more shortages: in 2012, 282 drug shortages were prevented, a 45-percent increase from the previous year.

FDASIA has been extremely helpful in assisting FDA in addressing drug shortages by requiring that manufacturers notify the Agency early if they identify issues that could lead to a potential shortage or a manufacturing disruption and to report the reasons for these issues. Notifications to FDA from manufacturers increased six-fold after the Executive Order was issued by President Obama on October 31, 2011, and they have continued at this heightened rate since enactment of FDASIA. Early notifications from the manufacturer to FDA are a key step in helping to prevent drug shortages. With the benefit of extra time, FDA can use mechanisms within its power to work with sponsors to resolve manufacturing and quality issues, expedite inspections and reviews of product submissions, determine if other manufacturers are willing and able to increase production, help sponsors qualify new sources of raw material, and in appropriate cases, review possible risk mitigation measures for remaining inventory.

For example, a company recently notified FDA of the risk of particulate matter in an injectable drug product needed for IV nutrition therapy. The particles were found to be foreign material from the manufacturing line, and, through ongoing communications with FDA, the manufacturer

was able to show that a filter successfully removed the particulate. FDA exercised discretion to allow distribution of the product along with a letter included in the drug's packaging, warning health care professionals to use a filter when administering the drug. The drug was available while the firm addressed the root cause of the problem, so that it could resume producing a drug that did not need the work-around involving the filter. FDA has exercised this type of regulatory flexibility while maintaining safety for important drugs several times over the past two years, including lifesaving components of IV nutrition for newborns, children, and other patients who are unable to eat and drink by mouth.

FDA is implementing the drug shortages provisions of FDASIA, including the publication of a Strategic Plan for Preventing and Mitigating Drug Shortages (the Strategic Plan), a plan that outlines our current actions as well as potential future directions for FDA and industry. Because it is clear that FDA cannot solve this public health threat alone, as a part of this work, FDA's Drug Shortages Task Force has sought input from a variety of stakeholders to help find solutions. The Strategic Plan includes two overarching strategies to address drug shortages: improving FDA's response to notifications received from industry to prevent a shortage (or where a shortage is unavoidable, to mitigate its impact on patients); and preventing the issues that are the root cause of most shortages, including efforts to promote and sustain quality manufacturing. The Strategic Plan is posted on FDA's website.[5] FDA also issued a proposed rule implementing the expanded early notification requirements included in FDASIA, and established a docket for the public to provide comment on the proposed rule.[6]

[5] http://www.fda.gov/downloads/Drugs/DrugSafety/DrugShortages/UCM372566.pdf
[6] https://federalregister.gov/a/2013-25956

Innovation

FDASIA gave FDA another powerful expedited development tool known as the "breakthrough therapy" designation. This tool is designed to expedite the development of new drugs based on preliminary clinical evidence that indicates the drug may offer a substantial improvement over available therapies for patients with serious or life-threatening diseases. The sponsor of a product with "breakthrough therapy" designation receives, among other things, the benefits of "fast-track" designation, as well as intensive guidance from the Agency on efficient drug development, beginning as early as the Phase 1 period. Breakthrough therapy drugs go through the same process for approval as other drugs; the program does not change approval standards. We have been very active on this subject, meeting with companies and discussing ways to expedite the drug development process for drugs that show striking early results.

FDA reviews requests for breakthrough designations within 60 days of receipt of the request. As of August 31, 2013, FDA had received 85 requests for breakthrough therapy designation, and FDA has already granted the breakthrough therapy designation to 27 potential innovative new drugs that have shown encouraging early clinical results in treating conditions, such as cystic fibrosis, epidermolysis bullosa, hepatitis C infection, breast cancer, Waldenstrom's macroglobulinemia, and Duchenne muscular dystrophy, to name a few. Many of the breakthrough therapy designations granted so far have been for rare disease indications. FDA has not yet approved any products for which a breakthrough therapy designation has been granted.

It is FDA's view that drug developers should have a clear understanding of all of FDA's expedited development and review tools, including breakthrough therapy designation, accelerated approval, the fast-track program, and priority review. To help industry better

understand each of these tools, including when the tool can be used and the features of each, in June 2013, we published a draft guidance for industry entitled "Expedited Programs for Serious Conditions—Drugs and Biologics."[7] Among other important information, the draft guidance describes FDA's policies and the threshold criteria and features for each expedited program, defines and discusses important concepts (including "serious condition," "unmet medical need," and "available therapy"), and provides general considerations for products utilizing an expedited program, such as manufacturing and product quality, non-clinical considerations, and clinical inspection considerations.

Development of Antibacterial Drugs

Recognizing the need to stimulate investments in antibacterial drugs, Congress enacted the Generating Antibiotic Incentives Now (GAIN) title of FDASIA to create an incentive system. The primary framework for encouraging antibacterial development authorizes FDA to designate human antibacterial or antifungal drugs that are intended to treat "serious or life-threatening infections" as "qualified infectious disease products" (QIDP). With certain limitations set forth in the statute, a sponsor of an application for an antibacterial or antifungal drug that receives a QIDP designation gains an additional five years of exclusivity to be added to certain exclusivity periods for that product. A drug that receives a QIDP designation is also eligible for designation as a fast-track product, and the application for that drug is eligible for priority review. Between July 9, 2012 (when the GAIN title of FDASIA went into effect) and September 17, 2013, FDA granted 24 QIDP designations. On June 12, 2013, FDA issued a proposed rule to establish a Congressionally mandated list of "qualifying pathogens" that have the potential to pose a serious threat to public health and made public the methodology for developing the list, as required by FDASIA.

[7] *http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM358301.pdf.*

Pediatrics

FDASIA strengthened and made permanent provisions to improve the safety and effectiveness of drugs, biological products, and medical devices intended for use in pediatric populations. It made permanent the Best Pharmaceuticals for Children Act (BPCA) and the Pediatric Research Equity Act (PREA), and authorized certain funding associated with pediatric device development. As we mark the 16-year anniversary of BPCA and the 10-year anniversary of PREA, we are pleased to report that, since passage of those important pieces of legislation, more than 500 drug labels have been revised to contain information about use of products in pediatric populations.

Under FDASIA, PREA was amended to require the submission of pediatric study plans, typically at the end of Phase 2. This provision provides an opportunity to improve the pace of pediatric drug development by requiring sponsors to submit pediatric study plans early in a product's development program; it is consistent with FDA's stated regulatory objectives and facilitates alignment with European efforts in the arena of pediatric product development. FDA implemented this provision in early January 2013. In addition, FDA has published a draft guidance to industry, "Pediatric Study Plans: Content of and Process for Submitting Initial Pediatric Study Plans and Amended Pediatric Study Plans."

Congress also provided FDA with increased flexibility and mechanisms to ensure the completion of pediatric studies required under PREA. Under FDASIA, FDA was given the authority to grant extensions of deferred pediatric studies under PREA. FDA has successfully implemented a process for review and granting of deferral extensions. As of October 1, 2013, 99 deferral extensions have been requested and 84 deferral extensions have been granted. FDA was also

given authority to issue non-compliance letters for failure to submit required studies under PREA. These non-compliance letters must be publicly posted. FDA began posting non-compliance letters for failure to complete PREA-required studies in August 2013. As of October 1, 2013, nine non-compliance letters were posted.

FDA is also working to address the lack of sufficient labeling information for neonates, by establishing a Neonatal Subcommittee of the Pediatric Advisory Committee and by entering into a two-year contract for a part-time neonatologist to assist FDA in establishing priorities and scientific pathways for product development for neonates.

FDASIA reauthorized grant funding for non-profit consortia to stimulate pediatric device development. The Pediatric Device Consortia (PDC) Grant Program funds consortia, which provide advice and device development resources to innovators in developing medical and surgical devices designed for the unique needs of the pediatric population—needs that often go unmet by devices currently available on the market. In FY 2013, FDA awarded PDC grants to seven consortia[8] supporting innovators in the pediatric device development space.

FDA has also issued a proposed rule,[9] as required under FDASIA, relating to the tracking of pediatric uses of devices, along with companion draft guidance.[10] This proposed rule would require applicants to include in certain premarket submissions readily available information about pediatric patients who suffer from the disease or condition that the device is intended to treat, diagnose, or cure. The information submitted will be used to help FDA better track the

[8] The recipients of the PDC Grant Program Awards for FY13 were: University of Michigan Pediatric Device Consortium, Atlantic Pediatric Device Consortium, National Capital Consortium for Pediatric Device Innovation, New England Pediatric Device Consortium, Southern California Center for Technology and Innovation in Pediatrics, Philadelphia Regional Pediatric Medical Device Consortium, and Boston Pediatric Device Consortium.
[9] *http://www.gpo.gov/fdsys/pkg/FR-2013-02-19/html/2013-03647.htm.*
[10] *http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm339162.htm.*

number of approved devices for which there is a pediatric subpopulation that suffers from the disease or condition that the device is intended to treat, diagnose, or cure. FDA would like to use this data to identify unmet pediatric needs in medical device development.

Rare Pediatric Disease Initiatives and Other Rare Disease Programs

FDASIA added a number of new provisions for rare diseases, including the rare pediatric disease priority review voucher program, consultation with external experts on rare diseases, and a pediatric rare diseases public meeting. Under PDUFA V, a rare diseases program in CDER and a rare diseases liaison in CBER were added.

The rare pediatric disease priority review voucher provision is intended to encourage development of new drugs and biologics for prevention and treatment of rare pediatric diseases. FDA has already designated one drug product as a drug for a rare pediatric disease and is reviewing several other designation requests. Designation is only one part of the voucher program. It does not guarantee that the sponsor will receive a priority-review voucher upon approval because voucher eligibility depends on the contents of the marketing application. FDA is working on a draft guidance that will explain the voucher eligibility criteria and the processes for requesting designation and a voucher.

FDA has already scheduled a public meeting, as required by FDASIA (specifically, PDUFA V), to discuss ways to encourage and accelerate the development of new therapies for pediatric rare diseases and to discuss complex issues in rare-disease drug development. This meeting is scheduled for January 2014. FDA is seeking input from academicians, clinical practitioners, patients and advocacy groups, industry, and governmental agencies on issues associated with drugs, biological products, and medical devices used for the diagnosis and treatment of pediatric

patients affected by rare diseases and on complex issues in rare-disease clinical trials. The input from this public workshop will help in developing a strategic plan to encourage and accelerate the development of new and improved therapies for pediatric patients affected by rare diseases.

For rare diseases generally, FDASIA reauthorized grant funding for the Orphan Products Grants Program. This program funds clinical trials involving rare diseases; i.e., diseases that affect less than 200,000 people in the United States. In FY 2013, FDA awarded 15 grant awards to boost development of rare disease therapies.[11] This year's funded studies have an emphasis on vulnerable populations, populations that are extremely difficult to treat, and populations that have no available options.

Unique Device Identification (UDI) System

On September 20, 2013, FDA announced the final rule for a UDI system, which, once implemented, will provide a consistent, standardized, unambiguous way to identify medical devices. The UDI system will be phased in over several years, focusing first on the highest-risk medical devices. Once fully implemented, the UDI system rule is expected to have many benefits for patients, the health care system, and the device industry. It will provide improved visibility as devices move through the distribution chain, enhancing the ability to quickly and efficiently identify marketed devices when recalled and improve the accuracy and specificity of adverse event reports; it will also offer a clear way of documenting device use in electronic health records and clinical information systems.

[11] The recipients of these grants include: Alkeus Pharmaceuticals, Inc., Children's Hospital Medical Center Cincinnati, Children's Hospital of Philadelphia, Duke University, Emory University, PNA Center for Neurological Research, Spineform LLC, Tufts Medical Center, University of Colorado Denver, University of Texas MD Anderson Cancer Center, University of Texas Medical Branch Galveston, University of Washington, and Vanderbilt University.

Investigational Device Exemptions

FDA is also implementing the provisions of FDASIA relating to investigational device exemptions (IDEs). FDA approval of an IDE is required for U.S. human study of a significant-risk device that is not approved for the indication being studied. CDRH has made changes to its IDE decision letters to align them with FDASIA's requirement that FDA may not disapprove a clinical investigation on the basis of its conclusion that the investigation may not support future premarket clearance or approval of a device, or that a different investigation may be necessary to support a premarket submission. In addition, on June 14, 2013, FDA re-issued a draft IDE guidance,[12] which incorporates the FDASIA requirements related to IDEs. In this guidance, the Agency proposes a voluntary process, called a "Pre-Decisional IDE," intended to enable a sponsor to obtain timely feedback from FDA on its IDE prior to a formal submission to FDA, in order to facilitate faster approval times for IDE submissions and to help address commonly reported challenges in the initiation of clinical trials. Also in the guidance, in an effort to promote timely initiation of clinical investigation enrollment that protects study subjects, FDA has developed methods to allow a clinical investigation of a device to begin under certain circumstances, even when there are outstanding issues regarding the IDE submission.

De Novo Device Classification Pathway

FDASIA also included provisions to streamline the *de novo* classification pathway for novel devices of low-to-moderate risk. Sponsors of these devices may now submit a *de novo* request for classification without being required to first submit a 510(k) premarket notification to FDA and receiving a "not substantially equivalent" determination. FDA is using its authority under this new provision to review "direct" *de novo* petitions from sponsors and, as of September 19, 2013, has initiated review of 33 such "direct" *de novo* device submissions. FDA

[12] *http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM279107.pdf.*

has also implemented process improvements to increase the efficiency, transparency, and accountability of the Agency's *de novo* review process. For example, we are encouraging utilization of the pre-submission process for sponsors to engage in active dialogue with FDA to further encourage efficiencies related to *de novo* review. In addition, decision summaries for *de novos* granted marketing authority through the *de novo* process are available on FDA's website.

Health Information Technology (Health IT)

Pursuant to section 618 of FDASIA, FDA is currently working with the Federal Communications Commission (FCC) and the HHS Office of the National Coordinator for Health IT (ONC) to develop a report that contains a proposed strategy and recommendations on an appropriate, risk-based regulatory framework for health IT that promotes innovation, protects patient safety, and avoids duplicative regulation. FDA, in collaboration with ONC and FCC, set up a working group under ONC's Health IT Policy Committee (HITPC) in early 2013 to gather input from a variety of stakeholders and experts to inform the HITPC's recommendations to FDA on an appropriate, risk-based regulatory framework pertaining to health IT; that working group held numerous, productive meetings on this topic. On September 7, 2013, the working group provided its final recommendations to the HITPC.[13] FDA, ONC, and FCC intend to use the input from the HITPC in the agencies' development of the report.

On September 25, 2013, FDA published its final guidance on mobile medical applications (mobile medical apps).[14] FDA issued the mobile medical apps guidance to provide clarity and predictability for manufacturers of mobile apps. This guidance informs manufacturers, distributors, and other entities about how FDA intends to apply its regulatory

[13] *http://www.healthit.gov/facas/calendar/2013/09/04/hit-policy-committee.*
[14] *http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM263366.pdf.*

authorities to software applications intended for use on mobile devices that perform the same functions as traditional medical devices.

Consistent with FDA's existing oversight approach, which considers functionality rather than platform, the Agency intends a tailored approach and to apply its regulatory oversight to only those mobile apps that are medical devices whose functionality is of a kind that FDA already regulates and that present a greater risk to patients if they do not work as intended. FDA has already cleared more than 75 such mobile apps since the late 1990s.

Device Modifications

On June 13, 2013, FDA held a full-day public meeting to obtain input from external stakeholders on when a modification made to a 510(k)-cleared device requires a new 510(k) submission. FDA will consider all comments and input from interested stakeholders, including comments received during the public meeting and submitted to the docket for the *Federal Register* notice announcing the meeting, when formulating FDA's Modifications Report to Congress and any future guidance on this topic. FDA also plans to seek public comment on the contents of the report prior to issuing any future guidance.

Class III "Preamendments" Devices

FDASIA changed the process for reclassifying devices and requiring premarket approval for Class III preamendments devices[15] from rulemaking to an administrative order process. FDA is using its authority under this new provision and has taken significant steps toward completing the Agency's ongoing efforts to finalize the classification process for Class III preamendments device types. We have issued proposed orders to finalize the classification of 13 Class III

[15] "Preamendments" devices are those devices that were in commercial distribution prior to passage of the Medical Device Amendments of 1976.

preamendments device types using the new FDASIA authority. As of October 1, 2013, FDA has either issued a proposed order, or finished classifying the device type through the rulemaking process, for all but six Class III preamendments device types. FDA continually updates our progress on the Class III preamendments devices through our publicly accessible "515 Project Status" webpage.[16]

Humanitarian Device Exemptions (HDE)

To encourage the development of medical devices intended to benefit patients in the treatment and diagnosis of rare diseases, certain devices for rare diseases or conditions may be granted an HDE, which allows the sponsor to seek FDA approval for the device by demonstrating only a reasonable assurance of safety and not a reasonable assurance of effectiveness. Previously, only devices approved under an HDE that were intended and labeled for use in pediatric patients after the date of the enactment of the Pediatric Medical Device Safety and Improvement Act of 2007 could seek to make a profit on their device. FDASIA broadened the circumstances under which a sponsor of an HDE-approved device could make a profit, in order to further encourage the development of medical devices for rare diseases and conditions without undermining the incentive for sponsors to develop these devices for pediatric populations. As of October 1, 2013, FDA has approved five HDE supplements for HDE device sponsors, taking advantage of this modified provision.

Other FDASIA Provisions

Pursuant to section 907 of FDASIA, on August 20, 2013, FDA released a report entitled "Collection, Analysis, and Availability of Demographic Subgroup Data for FDA-Approved

[16] *http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDRH/CDRHTransparency/ucm240310.htm.*

Medical Products."[17] To inform the Agency's follow-up action plan on this issue, FDA has opened a 90-day docket soliciting public comment on the report.

In accordance with Subtitle B of Title XI, on December 18, 2012, FDA issued draft guidance titled "Certification Process for Designated Medical Gases." FDA explained the certification process for designated medical gases in January 2013; this process allows certain medical gases listed in the statute for specific indications to be approved efficiently.

With regard to FDA advisory committees, FDA has continued to reduce the percentage of standing-member vacancies on the Agency's advisory committees. Between October 2012 and August 2013, the rate of such vacancies decreased from 22 percent to 16 percent. At the same time, the percentage of conflict-of-interest waivers granted to advisory committee members has remained low and is currently less than 1 percent.

CONCLUSION

Implementing FDASIA is a considerable undertaking, requiring detailed planning to integrate these tasks with the rest of FDA's workload. All told, the 140-page law called for multiple deliverables of all types, including more than 30 proposed and final rules, more than 40 draft and final guidance documents, more than 20 reports to Congress, and many other additional reports, assessments, public meetings, and plans. FDA continues to meet most of its FDASIA milestones and is on track to implement more provisions very soon. To help the public keep track of our progress on these and other provisions, we have established a FDASIA web portal[18] that includes a link to our three-year implementation plan, which we update regularly.

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[17] *http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM332136.pdf.*
[18] www.fda.gov/fdasia.

FDA is committed to implementing the requirements of FDASIA in a way that provides lasting improvements to public health, and we will meet these objectives as quickly as resources allow. We are happy to answer any questions you may have.

Mr. PITTS. The Chair thanks the gentleman. That concludes the opening statements. We will now begin questioning. I will recognize myself 5 minutes.

Before I begin, Dr. Woodcock, would you submit that spreadsheet for the record?

Ms. WOODCOCK. I will confer with my folks and see what I can send you. We definitely will give you something.

[The information appears at the conclusion of the hearing.]

Mr. PITTS. All right. And I have a number of questions for both of you that I will submit for the record. Would appreciate that you respond promptly.

Dr. Woodcock, we enacted FDASIA in order to bring greater predictability, consistency, and transparency to FDA's regulation of medical devices and drugs. FDASIA included some significant changes to the review process on the device and drug side. How have you translated the FDASIA policy changes into the regulatory review process? And how have you communicated these changes to your staff? How are you ensuring that your staff implements the law correctly?

Dr. Woodcock, you want to begin?

Ms. WOODCOCK. Well, some of the primary changes that we received, we negotiated with the industry under the PDUFA agreements for a new review program for new molecular entities. They are the most innovative drugs. We are now having midcycle meetings during the review process. So this mainly changes how we run the review process, allows for more communication between industry and the review staff during the review process. And it is hoped we can clear up any confusion, answer questions and so forth, and get to a complete response that includes all the issues at the end of the day.

So we are running that as a pilot. We are going have an independent assessment of that. We have had a number of new molecular entities that have been approved. I believe six have been approved that have gone through that program. So it is in its early stages, though, because we are going to run several years of the program and then evaluate its success.

And the other major change, of course, has been the breakthrough designation program, and I could talk about that if you want. So we have received almost up to 100 applications for designation under this program. We have designated more than 25 different products for a range of different diseases as potential breakthrough products. And we have just approved two, one last week and one on Wednesday. On Wednesday we approved a drug for mantle cell lymphoma, which is a rare kind of immune system or blood tumor.

So we feel this program has been fairly successful so far in bringing greater attention to drugs that are potential game changers for people with serious diseases.

Mr. PITTS. All right. Thank you.

Dr. Shuren, under MDUFA III industry and the FDA agreed to have an independent two-phase assessment and program evaluation to objectively assess the FDA's premarket review process. Can you explain how FDA was involved in setting the parameters of this assessment?

Mr. SHUREN. Certainly. We have put out calls for an independent contractor to perform the work, and that was assigned to—oh, my apologies.

We have put out a call to have an independent contractor perform the assessment, and Booz Allen Hamilton is that contractor. We worked on a draft statement of work which we put out to the public for comment. We had discussions with industry on what should go into that statement of work.

And then finally we have been overseeing the process for the contractor. We get updates on the progress they make. But it is independent, so we don't know what they are actually going to report to us. Our understanding is they have gone out, they have had conversations with stakeholders, particularly industry, they have conducted focus groups. And we are expecting to get their first report very soon, and we have a public commitment to make that available to the public in December, which we will do. And that first phase includes their at this point preliminary findings, a lot of their more of the low-hanging fruit. Six months thereafter, so in May, they will have the second phase, where we will get all of their recommendations. At that point, too, we have a public commitment to issue our plan for implementation of the recommendations.

Mr. PITTS. Would you agree to submit a detailed accounting of the agency's involvement with the contractor relating to the review and any recommendations or directions you provided them?

Mr. SHUREN. Yes, we can provide you with information.

[The information appears at the conclusion of the hearing.]

Mr. PITTS. And would you agree to submit a compiled list of recommendations in its entirety to the committee upon its completion?

Mr. SHUREN. We are going to make it available to the entire public.

Mr. PITTS. OK.

Mr. SHUREN. But we will include you on that, too.

[The information appears at the conclusion of the hearing.]

Mr. PITTS. All right.

Dr. Woodcock, the President's Council of Advisors on Science and Technology's September 12th report included specific recommendations on how the Federal Government might propel innovation in drug discovery and development. PCAST expressly recommended, quote, "It could be valuable for the Congress to establish that encouraging innovation and drug development is a clear component of the FDA mission," end quote.

Do you agree with the President's advisors that including innovation in the mission statement would be valuable?

Ms. WOODCOCK. Well, I think it is a double-edged sword. We don't encourage innovation for innovation's sake. OK? Innovation can end up being bad as well as being good, right? But innovation is essential to treat current unmet medical needs. So absolutely we should foster innovation and be open to it and allow new methods of both treating patients and manufacturing drugs to have progress. So I think it is really how you state that support for innovation that is important.

Mr. PITTS. All right. My time has expired.

The Chair recognize the ranking member, Mr. Pallone, 5 minutes for questions.

Mr. PALLONE. Thank you, Mr. Chairman.

My questions of Dr. Woodcock—first, welcome back. I can guess you have had quite a busy year. And I wanted to start today talking about the new Office of Generic Drugs. I was glad to see the decision FDA made last year to elevate the Office of Generic Drugs to a "super office" on equal footing with the Office of New Drugs within the agency. And as you know, I introduced a bill last year that included a provision to do just that and I have long been an advocate for the structural change within FDA to enhance the role of the Office of Generic Drugs.

I would like to ask you, Dr. Woodcock, whether the Office of Generic Drugs has officially been set up in its new elevated position? And how is it structured? What kinds of changes have been made? And when do you expect the change to be finalized?

Ms. WOODCOCK. The organizational change has been not finalized. We are in the final stages of that, and I hope it would occur very soon. What it will do is recognize the fact that generic medicines treat most people in the United States. Eighty-four percent of dispensed prescriptions are for generic drugs. And so the new generic drug office will have a much more clinical focus. We will have more doctors there, more clinical staff, very much focused on therapeutic equivalents, the adverse event reporting, making sure those generic drug labels are up to date and so forth.

So as a super office it is proposed to have a bioequivalence office, a research office, because under GDUFA we negotiated and received money so that we can do research to get new categories of drugs like inhalers to become generics, right? So they have a research office and then an office that will run the operations, including a clinical safety staff.

Now, as part of this, what we are proposing, though, is that quality regulation, drug quality regulation be reorganized and that we centralize that, and that is a plan that I am working very intimately on. And this would ensure that generic drugs, new drugs, over-the-counter drugs, any kind of drug we regulate have the exact same quality expectations across the industry.

Mr. PALLONE. OK. Then I wanted to speak about the FDA's progress in implementing GDUFA. I commend the FDA on meeting its GDUFA hiring goals for the fiscal year, and I know the difficulties associated with implementing a brand-new program. But how many FTEs have you hired to date and how many do you plan to hire in the first two quarters of next year? And given the backlog of pending ANDAs, can you give the committee an estimate on how many of these new hires will be dedicated to ANDA review? I have others, but let's start with that.

Ms. WOODCOCK. OK. We have hired upward of 300 people. I mean, that number changes every day. We are aggressively hiring. And we exceeded our GDUFA goal, which was 25 percent of the total number of people that were to be hired. OK?

We have acted on 900, I think, of ANDAs in the backlog in different ways, so we have reduced that pending backlog, but it is still formidable. I wouldn't diminish that. And we have done a lot of things to try and aggressively address this backlog. So your other question?

Mr. PALLONE. Well, I was going to ask you if the government shutdown affected the progress for those 2 or 3 weeks?

Ms. WOODCOCK. Well, the major effect on our review programs, because we were able to continue to operate under the user fees. However, the inspections stopped for those several weeks. So the inspectional programs were not operating. And of course that is one of the things that we really need to ramp up under GDUFA, is to increase the number of facility inspections that we do if we are going to tackle this backlog and get into a steady state.

Mr. PALLONE. And the last thing, it is my understanding that FDA recently advised sponsors that it has restricted communications with sponsors during the ANDA process. Specifically, rather than providing ongoing status updates, the FDA has a new policy of only providing approval answers. Can you explain the reasoning behind this, why you feel the need to have less communications than before, given that we have the user fee funds available?

Ms. WOODCOCK. We have upward of 8,000 items pending in the generic drug review program. The previous practice was companies would call all over the place to try to find their status. If every chemist and bioequivalence reviewer is answering questions from 8,000 different sites asking them what is the status, we are never going to get done.

So we are trying to bring order to this process, like we have for PDUFA, and what we want to do is have predictable deadlines so that every company knows their application is on track and going to get out of the agency and they are going to get a complete response within the timeframe that has been established under GDUFA.

So I think some of this is a transition issue where we are going from one state to another and we are going to have to get through this period. We are doing everything we can and we are considering additional steps to notify industry as their application approaches an action so that they can prepare, say, for launch or whatever they need to prepare for. We understand that need. However, we can't have companies' thousands of calls to reviewers or we are not going to get this program done.

Mr. PALLONE. All right, thanks a lot.

Mr. PITTS. The Chair thanks the gentleman.

We are presently voting on the floor. We will try to get through a couple more members. The Chair recognize Mr. Whitfield for 5 minutes for questions.

Mr. WHITFIELD. Well, thank you very much, and thank you all for joining us this morning.

Last April I attended a meeting with a group of dermatologists and they were talking about the approval process for over-the-counter in general and sunscreen in particular. And they had indicated that there were, like, eight sunscreen applications that had been at FDA waiting for a decision for, like, 10 years. Some of these have been used in Europe.

We all are very much aware that you all have a very heavy workload and you have limited resources. And I know in conversations with Congressman Dingell, and I know on the Senate side Senators Reid and Isakson have been discussing this issue, and Congressman Dingell and I have draft legislation to try to expedite

the process and we had submitted to you all for technical assistance. And I was going to ask, one, are you, with the multitude of issues you deal with, are you even aware of legislation that we have submitted? And if you are, could you give us any idea of maybe when we could expect a response from you?

Ms. WOODCOCK. We hope you would get a prompt response.

Mr. WHITFIELD. OK.

Ms. WOODCOCK. This is a very intractable problem. I think, if possible, we are more frustrated than the manufacturers and you all are about this situation. We have to do regulations to get these ingredients into the monographs. That is the problem. And they are backlogged and they are slow to get through, and we have to do a proposed regulation, sometimes we have to do advanced notice of proposed regulation, then do a proposed rule, and then do a final rule, which can take 6 to 8 years. And we have multiple categories of these over-the-counter products that we have to handle. But the sunscreens, there is a public health issue here.

Mr. WHITFIELD. Right. And who on your staff specifically can we be in contact with on the technical assistance?

Ms. WOODCOCK. Well, I think that our lead in this is Dr. Sandra Kweder, who is acting head right now of the office that oversees this, but, of course, work through our legislative staff and we will provide any assistance needed.

Mr. WHITFIELD. OK.

Mr. DINGELL. Would the gentleman yield?

Mr. WHITFIELD. I would be happy to yield.

Mr. DINGELL. Briefly. First of all, I want to thank the gentleman. Second of all, I want to commend him. And third of all, I want to note that this is important. This matter has been dawdling by prodigious overlong delay, and it has simply got to come to a halt. Your assistance would be extremely important. I want to work with my good friend. And I urge you to resolve this problem. It is a significant problem that does do the Food and Drug Administration no credit whatsoever.

Mr. WHITFIELD. I yield back the balance of my time.

Mr. PITTS. The Chair thanks the gentleman.

I think we can get one more in. We will reconvene shortly after the second vote. There are two votes. That will be about 11 o'clock. The Chair recognize the gentleman, Mr. Dingell, 5 minutes for questions.

Mr. DINGELL. Mr. Chairman, I would like to defer. I move rather slowly.

Mr. PITTS. All right. Then we will at this point recess the committee until after the second vote, and hope you will be patient with us. We will get back as soon as we can. Thank you. The committee is in recess.

[Recess.]

Mr. PITTS. The time for our recess having expired, the subcommittee will reconvene. And the Chair recognize the gentleman from Texas, Mr. Green, for 5 minutes for questions.

Mr. GREEN. Thank you, Mr. Chairman, for holding the hearing.

And, Dr. Woodcock and Dr. Shuren, thank you for taking time to be here today.

One of my top priorities is fostering a regulatory environment that would promote the development of the new antibiotic drugs to address the growing public health threat of drug-resistant bacteria. I am proud to have worked with leaders on this committee, Dr. Gingrey and a coalition of other members, to advance the GAIN Act last year. We have always said that this was a good first step, but more must be done. And I know from your testimony today that is true. Thank you for your leadership on the GAIN Act, Dr. Woodcock, and also promoting the new antibiotic development.

In April, CDC released a report on drug-resistant bacteria. In that report, CDC states that antimicrobial resistance is one of the most serious health threats to our country. Dr. Woodcock, does the FDA agree with the CDC on the nature of this threat?

Ms. WOODCOCK. Absolutely. We are very concerned about this.

Mr. GREEN. In this report, the CDC highlights a handful of strategies to address this threat. One of the main methods they suggested was to develop new antibiotics. As I understand it, part of the challenge of the new developing antibiotics is that drug resistance oftentimes begins in limited populations and approving a drug through the FDA for use in a limited population can be difficult.

Dr. Woodcock, on June 4th of this year you were quoted by the National Public Radio as saying that you hope Congress would pass legislation soon to make it easier for FDA to approve new antibiotics. What type of legislation were you referring to when you made those statements on NPR?

Ms. WOODCOCK. Well, there have been discussions, and the PCAST report referred to earlier—I am sorry. There have been discussions, and the PCAST report referred to earlier have talked about a program for limited use that is specifically directed where there is subpopulation of broader population. Because one of the problems we have with the antibiotics, as you well know, is overuse. And what we are concerned about if we approve an antibiotic for a limited use, just for drug-resistant organisms, that there would be temptation to use it more broadly and thus lose its effectiveness. And so we feel that it should be explored that Congress could make some kind of program that would really send a signal about limited use and then good antibiotic stewardship.

Mr. GREEN. Well, I am working on legislation with my colleague Dr. Gingrey, and meant to be the next step from GAIN, focused primarily on promoting antibiotics meant to be used in limited populations. Is there anything that you believe we should keep in mind as we draft this legislation?

Ms. WOODCOCK. Well, I feel that a strong signal from Congress to the healthcare community about stewardship would be extremely important. FDA frequently approves drugs for limited populations, but usually there isn't that sort of, let's say, an orphan population, there isn't that sort of temptation or ability to use it broadly in a much broader population.

So one of the main things is a signal from Congress that it is fine to do limited populations out of a broader disease with a very small development program, but then there should be that stewardship by the healthcare community to not use it more broadly.

Mr. GREEN. Well, and I know if you deal with any of the infectious disease specialties, they talk about that. And can we statu-

torily, because I know in medical practice a doctor can make that decision on their own, and that may be part of the problem. But you can't limit it to just, for example, people who deal with infectious diseases, I guess.

Ms. WOODCOCK. We feel that there shouldn't be an overt limitation like that, because it is not feasible. Patients come in, they have infections, there is a resistant strain circulating in the community, doctors should have the discretion to use appropriate antibiotics. However, I think a signal of prudence and stewardship would be a mechanism I think would be very effective.

Mr. GREEN. And I am almost out of time, but the other issue on that is we need to make sure we keep this, because what may be successful a year from now or 10 years from now, we will still have people who develop those resistance, so we need to keep that pipeline going for these new levels of antibiotics and other ways to treat these terrible illnesses.

As health care gets more advanced and threats to our health get more complicated, it is important that both Congress and the FDA be responsive to this changing world. Many of the processes at FDA are decades old. Drug resistance, medical software, and personalized medicine are going to strain the limits of the outdated statute. I hope we can work together and have FDA as an active partner when we are drafting this and protect not only public health, but foster that innovation we need for that long term.

So, Mr. Chairman, thank you for your time.

Mr. PITTS. The Chair thanks the gentleman.

Now recognize the vice chair of the committee, Dr. Burgess, for 5 minutes for questions.

Mr. BURGESS. Thank you, Mr. Chairman. I apologize I wasn't here earlier. I had some obligations on the House floor.

I do want to take this opportunity just to recognize the fact that this subcommittee, and in fact the Energy and Commerce Committee as a full committee, did its work in what was sometimes a very difficult election year of 2012. Food and Drug Administration reauthorization of user fee agreements was going to expire. All of the people who write in the important papers around town said we couldn't do it. And you and Mr. Upton did it. The bill went through regular order, passed the subcommittee, passed the full committee, went over to the Senate, conference with the Senate, and the President signed it into law on July 9th of 2012. No one knows that because there was no signing ceremony and there was no press present. But Congress, when pressed, can actually function in a very reasonable way.

Dr. Woodcock, as you will recall, during the reauthorization discussion, actually I worked with Ranking Member Pallone on the concept of the advisory committees to make certain that they were staffed with the very best experts to serve patients well, serve you and your agency well, and reduce backlogs and save resources. And so it looks to me like the initial thing, reports I am getting are good. Do you have any updates for the committee today?

Ms. WOODCOCK. Yes. We have been able to remove several steps that were very time consuming within the vetting of the advisory committee process for members for a specific committee. That has helped us streamline that program. Of course, all advisory com-

mittee members are still subject to the broad Federal conflict of interest requirements, and that is, you know, fairly stringent as well. But the additional steps have been removed, and that has been helpful.

Mr. BURGESS. And sometimes it is helpful to have someone on an advisory committee who actually has some knowledge of the pathophysiology that might be involved in the disease under which we are contemplating treatment? Would that be a fair statement?

Ms. WOODCOCK. I would say it is essential.

Mr. BURGESS. I think so, too.

Now, there is going to be a rare disease meeting in January of this year. Is that correct?

Ms. WOODCOCK. I believe so.

Mr. BURGESS. And looking forward to improving the regulatory process for approving drugs for rare diseases. You held a similar meeting in 2010 and issued a report with recommendations. Can you kind of update us as to the implementations of those recommendations made 3 years ago in advance of this next meeting in January?

Ms. WOODCOCK. Well, I think we are doing extremely well on rare diseases. We have established a rare disease staff. We are tracking all the rare diseases. In 2013 we approved a large number of products for rare diseases. Every one of them was approved based on a surrogate in fiscal year 2013. That is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12 were products for rare diseases. And then one was approved on an animal rule without human efficacy testing. So we do have a robust program, and we are going to try to take it to the next level as we have more meetings, public meetings.

Mr. BURGESS. Dr. Shuren, as you know, for some time I have been interested in the research use only application. And there is recent guidance put out by your department that only products that could significantly restrict patient access and restricting sales of these products. Is there any evidence out there of patients being harmed by research use only products?

Mr. SHUREN. Well, we do have evidence of companies who are putting those products out for research use only, but actually promoting them for clinical diagnosis in cases where those research use only, because they are research use only, haven't been shown necessarily to be accurate. And in times where we have taken action, it is predominantly where there is an already available approved or cleared test that would be there as an alternative.

We have recognized some of the concerns, I will tell you, with the guidance. And one of the things in there was about putting on the makers of research use only that they should reasonably know about the people they are selling it to and their intentions. That is something we heard loud and clear. I want too tell you we have heard those comments. That will come out of the final guidance. And that final guidance will come out probably by the end of this month, and we will get you a copy of that, too.

Mr. BURGESS. And I appreciate that. But specifically, do you have evidence that patients have been harmed by using the research use only designation?

Mr. SHUREN. I am not aware of a specific patient for one of those. I don't know. We can look a little bit further.

Mr. BURGESS. Thank you. And I would appreciate your further investigation of that.

Finally, Dr. Woodcock, I just have to ask a question. January 1st of 2012 I lost access to a low-cost over-the-counter asthma inhaler. When am I going to get it back?

Ms. WOODCOCK. Well, I can't talk, as you know, publicly about applications that might be pending and so forth. But certainly that monograph status remains. And we certainly heard your concern.

Mr. BURGESS. Thank you.

Mr. PITTS. The Chair thanks the gentleman.

And now recognize the gentlelady, Ms. Castor, for 5 minutes for questions.

Ms. CASTOR. Well, thank you, Mr. Chairman.

And welcome. Dr. Woodcock, in September, in Tampa we had the BioFlorida Conference with researchers and device manufacturers and folks that are developing drugs come from all across the State. And FDA was kind enough to send Dr. Richard——

Ms. WOODCOCK. Moscicki.

Ms. CASTOR. Moscicki, thank you, from the Center for Drug Evaluation and Research. And I want to thank you very much, because it is, I know, the budgets are very tight, but to have folks that are leaders at FDA be able to interact directly with the folks in my State was greatly appreciated. So thank you. And the conference focused a lot on the future of drug approvals.

So we are pleased that the Federal laws are working well. I think the number one fear of everyone, the topic of this conference turned to sequestration, because people are rather surprised that even though FDA relies a lot on user fees, the user fees are subject to sequestration. This is not smart.

Some of the analysis I have seen, and tell me if these numbers are right, that to your budget, I don't know if this is the entire FDA budget or just your section, that in fiscal year 2013 you were subject to sequestration of $209 million. And on top of that, $85 million in private funding, the user fees, were sequestered at the same time. And then in fiscal year 2014, if the sequester is not replaced, you are looking at a cut of $319 million. And $112 million of that, or you can explain that, on top of that or as part of that is the private funding user fees.

I mean, this has got to have a harsh impact on development of new therapies, on review of devices, on review of innovative drugs. Tell us what you are facing now in your shop.

Ms. WOODCOCK. Well, the sequestration has been very difficult. Of course, it cuts the appropriated support for these programs as well as where there are use fees, some of the user fee programs have been subject. My understanding is that total for user fees has been $79 million in the last fiscal year. But, frankly, how these are calculated is above my pay grade, all right? But what certainly has happened, there are user fees that we are not able to access, across the device and the PDUFA program, and that would continue.

And what happened with PDUFA, we negotiated and the bill was passed. It recognized the new agreements on rare diseases, patient-focused drug development, and these other programs. And then the sequester removed practically the whole amount that was nego-

tiated for these new programs, these patient-focused programs, and other programs.

Now, we have put on the patient-focused drug development meetings regardless, but our implementation of our rare disease staff has been delayed because of the sequester, and similarly with a number of the other programs that we agreed to.

Ms. CASTOR. So that is not good news for families across the country, families with rare diseases that rely on your agency. It seems like we have taken a step forward with the Federal laws that have given you certain authorities and expanded user fees, but then it seems like on the other hand sequestration, brought by the Congress, is going to handicap you. I mean, this is a bad time to shortchange FDA. Can you characterize what it means, where you are very concerned? And I would assume you would recommend that sequestration be replaced going forward.

Ms. WOODCOCK. Well, as I said, the whole financial issues are above my pay grade. That is really up to Congress. However, we are in a threshold, and I think with devices, too, of a revolution in biomedicine, and we are starting to see the benefits of that. And we need to have the programs that can respond to that, and also programs that can get for those older drugs, get low cost, affordable generics out on the market promptly, and at the same time, shepherd those innovations, both devices and drugs, that are going to make a difference for people who are still suffering from untreatable diseases.

And we really, I passionately feel we have to deliver this to the public. We have to make sure our regulatory programs are up to the task of dealing with drug-resistant organisms, of dealing with the new science that is coming forward.

And we are always close to the bone, as you know, in FDA. We have to shepherd our resources very carefully. More is at stake here than just having our staff. What is at stake is are we going to translate these innovations into benefit for the public.

Ms. CASTOR. Thank you.

Mr. PITTS. The Chair thanks the gentlelady.

Now recognize the gentleman from Illinois, Mr. Shimkus, 5 minutes for questions.

Mr. SHIMKUS. Thank you, Mr. Chairman. I am glad to follow my colleague from Florida, because obviously history, it is interesting in that this was the President's proposal to go into sequestration. It was passed by the House. I voted for it. And the real way to solve sequestration is understand debt, deficits, and our entitlement programs, and get those reforms.

My fear for any agency, that without that the expansion of our entitlement programs is going to squeeze out the discretionary budget, whether that is the military, whether that is your agency. And the sooner we as a Nation own up to that, then we wouldn't be having this debate.

One of the great things I love about the job of being a Member of Congress is working with our constituents. So right during votes I had one of my constituents go, and we measured the Ohio clock, because I have a constituent who is building a replica. So we were tape measuring and stuff. So that is an example of kind of the things that we do.

And it is just lucky that you are testifying when I was approached by a constituent, a member of my church. And so I am going to get a privacy release statement and we are going to follow up with the FDA, but he was supposed to be in clinical trials in September. They have not been called. He has asked me to ask why. So if you all would just be prepared for when we get involved with that, I would appreciate that on behalf of my constituent.

So having said that, really my questions are to Dr. Shuren on the 510(k), some issues revolving with that, which I have been trying to follow closely. Many companies are providing us feedback that they are experiencing a significant shift in requirements for various 510(k)s. Particular concerns have arisen about new requirements being communicated by the FDA during the 510(k) review that go beyond previously sufficient data requirements.

If true, this concerns me because in many instances FDA has not issued any new guidance on public communication regarding policy changes. So the question is, has the FDA changed its data requirements for submission types without issuing updated guidance documents? And if so, can you tell me why the change in consistency?

Mr. SHUREN. Well, first of all, I will say that oftentimes if we are asking a company for additional data, sometimes it is in response to the data they provided to us, that there may have been issues in what was submitted.

One thing I will ask you is, if you have companies who believe that something has been changed and changed inappropriately, you are very welcome to send them to me directly, and I promise you I will look into it.

Mr. SHIMKUS. Thank you.

At hearings in this committee prior to the enactment of FDASIA you acknowledged that in some cases the CDRH reviewers were asking for data to support product applications that they should not be asking for. You also indicated in an October 2011 document that you planned to work on training reviewers to avoid these sorts of data requests. Can you give us an update on this and what steps have you taken to address this?

Mr. SHUREN. So we have taken a variety of steps to assure that the questions that we ask are need to know rather than nice to know. And I will tell you even from our own analysis it is not common, but it happens, and it concerns us.

So one of the things we have done is we have been reorganizing in our premarket review offices, and thanks to MDUFA III we have been bringing in additional managers for more oversight of the process. We have changed policies and procedures to put more checks into the system.

Under MDUFA III, we have also put in a back check. So with our high-risk devices, we actually have a dedicated staff who will review any and all major deficiency letters that go out for accuracy and appropriateness. We have biweekly premarket review rounds, where if issues get raised we are dealing with them with the reviewers and the managers at that point. And of course we have done training for everyone for starters.

Mr. SHIMKUS. And I will end up on this. What, if any, consequences are there for reviewers who ask questions beyond what is appropriate? And are those annotated on their performance re-

view evaluation so that if it happens numerous times? Many of us have been managers of personnel. And, you know, the reality is you have got to document, document, document, especially on a Federal employee who may not be responding to the proper directions.

Mr. SHUREN. Well, I will first say, and I am going to put this in because my folks get sometimes a hard rap, they are a great group of people. They are very smart, they are dedicated, and they have been working exceptionally hard to implement FDASIA and to make changes. And I think it is reflected, quite frankly, in our premarket review numbers. The bottom line is our performance is getting better, and it is getting better for the first time in a decade of worsening, and that is a lot of credit to them.

Making changes is hard when it is a large organization, and there are going to be blips along the way. And it is our responsibility to keep good oversight in the center. And when things do arise, we do engage with the individual. We try to educate and work with them and keep on top of it.

Mr. SHIMKUS. If the chairman would for just a follow-up, of course, annotating if there is numerous examples and writing it down is part of a good personnel status. So I hope you would consider and do that.

Mr. SHUREN. Yes. And I will say for anyone who is not performing appropriately, and that goes for anything, then appropriate documentation in the file, and also discussions with the employee, because you always want to, if an employee isn't doing well, to try to help them to get back on par with performance.

Mr. PITTS. The Chair thanks the gentleman.

And now recognize the gentlelady from California, Ms. Capps, for 5 minutes for questions.

Mrs. CAPPS. Thank you, Mr. Chairman.

And thank you to our witnesses for being here today. I am so pleased that we were able to reschedule what I consider to be a very important hearing. And I am very pleased that FDASIA included parts of my Sentinel Assurance for Effective Devices Act, also known as the SAFE Act, in its final form.

One section of that bill was to ensure swift release of the UDI, the unique device identifier rule, for public comment to improve device tracking and aid in any potential recalls. So, Dr. Shuren, I want to commend you for getting the final rule out on UDI. I know it has been a long time coming, and I am glad that you finalized it so things can finally move forward.

One concern we have heard from consumer groups has been that the final UDI, unique device identifier—I want to make sure people know what I am talking about—rule does not require the identifier to actually be on the individual product itself. Can you explain the decision to not require the UDI to be on each one of these products?

Mr. SHUREN. One of the principal drivers was cost, cost to the companies. And we want to make sure that in implementing and putting forward this important regulation that we keep in mind what the burdens may be for companies to try to comply. So that was the major reason.

We do still keep in marking the devices in really one exception, and that is if you make a device that is going to be used more than once and it is going to be reprocessed. Because in that case, the la-

beling that came along with the product that had the UDI got thrown away, now it is moving over to someone else, and you wouldn't know what that device is unless you marked those devices. And that is a requirement in the rule.

Mrs. CAPPS. OK. OK. That is good to know.

My SAFE Act also built upon the existing Sentinel program at FDA, a program that enables FDA to actively query automated healthcare data to evaluate possible drug safety issues quickly and securely. The SAFE Act, and section 615 of FDASIA, both broadened that usage to the medical device space, which will benefit producers and consumers alike by catching problems early and ensuring that data, not conjecture, but data determine our device safety policies.

Unfortunately, the rollout of Sentinel on the drug side has taken many years, more than many in the field think is necessary. So I hope that expansion to the device side will not be plagued with the same delays. And can you each give me a brief update on where the agency is with Sentinel? I would appreciate a longer update for the record.

[The information appears at the conclusion of the hearing.]

But just quickly, can you also explain for us how UDI fits into FDA's postmarket surveillance of medical devices? Will it be good for patients and for providers and for manufacturers?

Mr. SHUREN. So the UDI is absolutely essential. It is a condition precedent for having Sentinel for medical devices. And the reason is right now it is very hard to link a device with a patient's experience with that device in electronic health information, electronic health records. Unlike drugs, which had a new drug code that they could use right away, we didn't have anything for devices. So the UDI we need to have in place. And that is going to take a few years.

But in the interim, what we are also doing is the following. We are identifying, helping to develop new and validating tools for active surveillance, being able to go through information to find out what are better understanding of benefits, risks, and problems with devices, And we are working with our conflicts in CDER on that.

Also, Sentinel will be part of a broader National Medical Device Postmarket Surveillance System. So electronic health information and registries will be the backbone. And we view this not so much as an FDA system, but truly a national system to meet the needs of industry, healthcare providers, insurers, FDA.

So moving forward, the Brookings Institution is very soon going to call for the creation of a multistakeholder planning board to start to lay out the governance structure, policies, and procedures for such a surveillance system, which we think is important not only for identifying problems, but being able to use postmarket information to help lower burden and better inform decisions on premarket approval, help products get to market, help doctors and patients make better-informed decisions.

Mrs. CAPPS. Thank you very much.

And finally and briefly, another piece of FDASIA was a key component of my HEART for Women Act, bipartisan legislation that focused on doing all we can to address women's heart health and address health disparities. Section 907 of the FDASIA required an ex-

amination of the extent to which data on how approved medical products affect women, minorities, and ethnic groups be collected, analyzed, and publicly reported. This is an important step, but concerns persist I know, and I will be submitting many questions for the record, and I appreciate your team's attention to this matter.

And I don't think there is much time for you to respond. I just wanted to put that out. We will follow up with you. Thank you.

Mr. PITTS. The Chair thanks the gentlelady.

And now recognize the gentleman from Pennsylvania, Dr. Murphy, 5 minutes for questions.

Mr. MURPHY. Thank you, Dr. Shuren and Dr. Woodcock. I appreciate you for being here today.

I would like to take just a moment to ask you about an important medical device issue, although it was not part of FDASIA. The FDA has regulations about proper maintenance of complex medical devices such as radiation therapy and imaging equipment, and manufacturers are required to recommend maintenance standards to hospitals and physicians and collect data on how that equipment is kept and serviced.

My understanding is that the Center for Medicare and Medicaid Services may issue guidance telling hospitals they are free to vary from the manufacturer's maintenance recommendation on these types of devices. But we are not dealing with an automobile or refrigerator here. These are highly specialized pieces of equipment. And when a medical device is improperly serviced, the consequences can be pretty deadly, as you know.

When a New York Times series in 2010 raised concerns about patient deaths from improperly calibrated diagnostic and therapeutic equipment, this committee held hearings in the matter. I am concerned that weakening of equipment maintenance standards could have some severe consequences for patient safety, and the party responsible for that device is the manufacturer. If something goes wrong, it is that company's name on the label, even though they are not the ones that made the maintenance changes. I believe the FDA has weighed in on this possible action by CMS. Is that true, Dr. Shuren?

Mr. SHUREN. Yes, that is true.

Mr. MURPHY. Can you discuss the FDA's position on this and you concerned about anything there?

Mr. SHUREN. Our concern is that the maintenance schedule is really part of assuring that that device remains safe and effective. And we work with the companies on what is the appropriate maintenance schedule to assure just that. And as you mentioned, these are technologies that may be emitting radiation, and we want to make sure not only are you getting accurate images of patients, you want to make sure they are also getting the right amount of radiation, not too much. And so a good maintenance schedule is essential. And that is why we had raised certain concerns and shared those with our colleagues at CMS.

Mr. MURPHY. OK. Let me ask another issue here. And I will gave you a little briefing material on this a little bit ago, but I want to make sure we have it in the record. We are all concerned about hospital-borne infections. E. coli, MRSA, and other infections which spread in hospitals are particular risks for people in hospitals, par-

ticularly in an ICU, or people who are immuno-compromised, et cetera, in transplant patients, et cetera, and that people use substances that are put into paints and plastics and clothing to try and reduce infections. But there also is the element of copper, which in research I understand has shown that basically E. coli, MRSA, and some other diseases are killed in minutes, whereas those same diseases can last for weeks on plastics and stainless steel.

The EPA has said that any sort of regulation on this is in the FDA's hands and they are not going to do anything about it, even though they have other jurisdiction over copper. I wonder how this will work at the FDA in terms of expediting this. I mean, it is obviously not a new element. It has been around for billions of years. And it seems to me it ought to be something we can use, copper itself, or copper-nickel alloys and other alloys which we know that can be on handles, on trays, on other equipment and supplies where these diseases can be killed right away.

Can you comment on the procedures you could take on this? And could anything be sped up on this process?

Mr. SHUREN. So we are happy to look into it. If it is a medical device and it has copper on it, if it has an anti-infective, that is something that my center would generally take care of. If it is not on the medical device, so it is just the anti-infective, it tends to work by a chemical action, becomes a drug issue. And that is why if there is a company or companies dealing with it, it is important that we connect so we figure out exactly what we are trying to do and help them as best we can.

Mr. MURPHY. Just help me understand this, because I want to make sure we handle it in the right way. So if it is a door handle or a touch plate entering an ICU, if it is a switch plate in a hospital room, would those be medical devices or would they be———

Mr. SHUREN. So a lot of those basics oftentimes are not.

Mr. MURPHY. What category would they be in?

Mr. SHUREN. If you are talking about surgical instruments, you are now getting into———

Mr. MURPHY. I understand that. I understand that. So what category would they be in? Because the EPA is saying that FDA has to approve them.

Dr. Woodcock, do you have———

Ms. WOODCOCK. They would only considered a drug if they actually had a disease claim in humans. And we don't usually regulate door knobs as drugs, all right. I think we are talking about some jurisdictional, like, murkiness here that we would need to sort out.

Mr. MURPHY. Well, I would just hope. Let's put that on the record. We will get you the information on it. But I hope that is something that you and the EPA can discuss fairly quickly. Obviously, the 100,000 people who die every year from hospital-borne infections and the fifty billion dollars we spend, if this can be reduced by several, then we ought to work together.

Thank you so much. I appreciate it.

Mr. PITTS. The Chair thanks the gentlemen.

Now recognize the gentleman from New York, Mr. Engel, 5 minutes for questions.

Mr. ENGEL. Well, thank you very much. And welcome to both of you. Followed both of your work. And thank you for your service.

I believe that the good work done by this committee on the Food and Drug Administration Safety and Innovation Act was likely the best healthcare-related legislating done by Congress last year. A little more than a year after its passage, I am pleased that this hearing is taking place so we can continue to monitor the implementation of this important bipartisan law.

I have always fought for those with rare and orphan diseases. I am the author of the ALS Registry Act, and both the Paul D. Wellstone Muscular Dystrophy Community Assistance Research and Education Amendments of 2008 and 2013, which I have done with Congressman Burgess. I am particularly interested in the development and approval of drugs for rare diseases.

Therefore, one of the aspects of FDASIA I am most interested in is the improvements made to the accelerated approval pathway as part of the law. To me, diseases like muscular dystrophy are why the accelerated approval pathway is so important. Duchenne muscular dystrophy is the most common lethal genetic disorder of children worldwide, affecting one in every 3,500 live male births. There is no cure. It is always fatal. And the best hope for those with Duchenne is to treat the symptoms and delay its progression. I have a group of people in my district that called this disease to my attention.

However, in recent years the Duchenne research pipeline has held much promise, as potentially life-saving therapies appear on the horizon, making elements of FDASIA particularly relevant to this research community. Earlier this week, the FDA informed Sarepta Therapeutics that its experimental drug for Duchenne muscular dystrophy was not a candidate for the accelerated approval pathway at this time. I recognize that since Sarepta has not filed its new drug application most of the discussions between Sarepta and the FDA are confidential. But I hope that Sarepta will continue to pursue their treatment for Duchenne muscular dystrophy, and I hope that the FDA will continue to provide clear feedback to the company as they move through their various clinical trials.

So, Dr. Woodcock, can you elaborate on how you envision the enhanced accelerated approval pathway working?

Ms. WOODCOCK. Certainly. As I said, in fiscal year 2013 we approved a large number of rare diseases, and all of them were based on surrogate end points, which is the foundation for accelerated approval. However, we granted a number of them full approval because we felt enough information had been provided that a confirmatory trial would not be necessary.

So we certainly are using the accelerated approval in rare diseases. And what the FDASIA instructed us to do was to really consider additional end points, including intermediate clinical end points, in other words clinical end points that are reasonably likely to predict clinical benefit, and we intend to do that.

Mr. ENGEL. Thank you. Let me ask you another question. Recognizing the challenges in developing therapies within the rare disease space, how is the FDA working with companies to ensure proper parameters for success and failure are being established

through the clinical trial process in order for experimental medications to possibly be considered under the accelerated approval pathway?

Ms. WOODCOCK. We try to work one by one, because of course each one of these diseases is different. One of the most important things that can be done by the patient communities is to establish a natural history of the disease through data so that we understand and can predict what will happen. If there is an intervention, you can calculate how many patients you need in your trial and so forth.

And this hasn't been done before. And so we have really been pressing on that, and I think we have seen a lot of progress. But we work with the companies one by one to help them design their trial. And as I said, we have set up a rare disease staff, although that has been inhibited because some of that money has been influenced by the sequester.

Mr. ENGEL. Well, thank you. And let me talk about the sequester and building on what Ms. Castor asked. I didn't vote for the Budget Control Act of 2011, thankfully, which created this huge sequestration mess. I am very frustrated that the user fees paid as part of agreements reached in FDASIA are being sequestered. So why don't I ask Dr. Shuren, can you talk about how sequestration impacts the ability of the FDA to meet goals agreed upon as part of FDASIA?

Mr. SHUREN. It is making it challenging. I mean, we are meeting the goals now. But in 2013, we saw about an 8 percent cut. Critical funding for training of our staff, of our review staff who we want to be on top of cutting-edge technology. Saw a 15 percent cut in our ability to recognize national and international standards, which provides predictability for industry. We had a 50 percent cut in our investment in regulatory science to have better tools for assessing medical devices faster and at lower cost, which is a big deal for industry. And I had to shift 50 percent of my operating dollars into payroll in order to hire the people I committed to hire under MDUFA III.

So most of my extra money, if you will, beyond paying for employees, is to pay for the rent, keep on the lights, put money in the photocopier. I have very little to actually put in to really improve a program that still needs a lot of help. And if we go into 2014 and this continues, I am not going to have the money to be able to hire and maintain the people we committed to hire and maintain under MDUFA III. It is a big deal for us.

And sequestration, it is important on user fees. Most of our program is still funded by appropriated dollars. And those cuts, they are killing us. And we are a program, like drugs, where years before trying to actually turn the program around, and this is making it very challenging for us to do that.

Mr. PITTS. The gentleman's time has expired.

Mr. ENGEL. Thank you.

Mr. PITTS. The Chair recognize the gentleman from Virginia, Mr. Griffith, 5 minutes for questions.

Mr. GRIFFITH. Thank you very much, Mr. Chairman.

Dr. Woodcock, greatly appreciate the passion you showed earlier in your testimony. I would agree with you on that passion, particu-

larly about bringing innovative treatments for rare and terminal diseases. I have a little bill that would allow folks to get early access or early approval to those drugs in order to help them, and what we believe will actually lower the costs of some of that experimentation. We will talk about that another time.

I do want to talk about a bill, I know what we are doing here today is important, but I do want to talk a little about a bill we have waiting over in the Senate. The House passed the Drug Quality and Security Act. It was a bipartisan, bicameral compromise to prevent another fungal meningitis outbreak like the one associated with NECC's tainted sterile products, where we had 64 Americans unfortunately died as a result of that situation.

I am proud of the legislation that I worked on with Congressmen Gene Green and Diana DeGette. Ultimately, although we had a different package originally, we came to a compromise with our Senate colleagues and with your agency, and I look forward to the Senate getting around to it. It is held up for other reasons, but I look forward to the Senate passing the bill and it being signed into law.

And I am committed to engage in oversight to make sure that patient safety is being properly protected. I also look forward to the agency developing the notification system that Congressman Green, Congresswoman DeGette, and I authored to ensure that the FDA works more closely with those State boards of pharmacy to prevent another public health crisis.

That being said, there were some areas that we thought we might be able to get fixed that we didn't in that bill that have raised some concerns. And I would like to ask you about those in regard to that Drug Quality and Security Act. In its previous draft guidance the FDA recognized the importance of maintaining an office stock of compounded drugs that doctors can readily access and administer to patients in their offices. Can we rely on the agency to continue to allow doctors and hospitals to order and keep compounded drugs on hand for office use?

Ms. WOODCOCK. Well, we are going to have to see what is in the final bill, if it is enacted. And then as I understand it, it really removed the court disparity, which I didn't fully understand, but was a problem. And so it leaves the previous statute more or less intact, and we can implement it aggressively. And obviously, that is one of the considerations in there, is what are the four walls of what is Federal, what is State, and what is permitted.

Mr. GRIFFITH. And we didn't change anything in regard to office use, and so there is some concern that maybe we should have put it in. It was compromised that we would just leave it silent. And I hope that we can count on the FDA. I know you maybe can't answer that today. But I would hope that we can count on the FDA to leave that part of it that was working very well, which the FDA had previously done, leave that intact, because I don't think there was any intention, certainly not on our side, that that be changed in any way.

Likewise, repackaging of sterile drug products has typically been regulated by the agency in the same fashion as compounded drugs. Repackaged sterile drugs are vital for many patients, especially those in ophthalmologic health issues. Likewise, can we rely on the FDA not to go in and create chaos, and to preserve the access to

these repackaged sterile drugs and limit the impact of burdensome regulations on that practice?

Ms. WOODCOCK. Well, our intent certainly is not to create chaos.

Mr. GRIFFITH. Yes, ma'am.

Ms. WOODCOCK. All right? I think one of the goals, mutual goals, is to prevent contaminated drugs. And that is really our goal, and your goal as well, I believe.

Mr. GRIFFITH. It is. There were some clarifications that everybody decided to let go and hope that it works out. And so I am just worried about those areas.

The last of the three that I have is the nuclear pharmacists. They compound drug products that have a short radioactive half life and must be quickly delivered to a healthcare entity for administration to a patient. Sometimes this must be done in advance of a patient-specific prescription. Can we rely as well on the FDA to continue to try to monitor that in the same fashion that they did before this bill was passed? And I know that the Senate is either going to pass it today or next week. But anticipating that, since it was a compromise worked out between the two bodies and the FDA, what are your thoughts on that?

Ms. WOODCOCK. Well, the nuclear pharmacies have not represented a problem here. We have a scheme with them. We have been very successful in implementing a regulation of positron emission tomography facilities, and that has gone very well. And so I think we should continue along that path.

Mr. GRIFFITH. And I appreciate that greatly. And I would be remiss, you know, it is good to see a witness with passion and your dedication. We may not always agree on how to get there, but I always appreciate the fact that you come in with honest answers and a willingness to try to work things out, and I appreciate that.

Ms. WOODCOCK. Thank you.

Mr. GRIFFITH. With that, Mr. Chairman, I yield back.

Mr. PITTS. The Chair thanks the gentleman.

And recognize the gentleman from Maryland, Mr. Sarbanes, 5 minutes for questions.

Mr. SARBANES. Thank you, Mr. Chairman.

I just want to pick up on the end of those comments, and thank you, Dr. Woodcock, for being here, and say you are one of the most professional and knowledgeable witnesses we have the pleasure to bring before this committee from time to time. I thank you for your testimony, and yours as well, Dr. Shuren.

And I want to thank the chairman for convening this panel today and the committee hearing so we can get a sense of how things are progressing. These days, sort of bipartisan legislation that we all get behind is hard to come by, so it is nice to have the opportunity to hear that good things are already resulting from the passage of this reform, and we appreciate your testimony in that respect.

I was going to ask as well about how the kind of user fee resource has gotten caught in the switches of sequester, which I think you have answered that. It is particularly jarring I think to the industry, the notion that they are putting forward through the user fees resources from the industry, and even that gets implicated by the sequestration that has been put in place. And hopefully, we can address that for all the reasons that you have raised.

I don't have a lot of questions necessarily on the topics you have been covering because I think you have done a good job addressing them. I did want to ask something slightly off topic, which is, as a result of redistricting in Maryland, I now have the privilege of representing some portion of the White Oak facility and had the opportunity to get a tour recently and see the tremendous facilities that are provided there. And I wondered if you could just speak to the benefits of now being able to collocate so many of the FDA personnel and have the labs there near each other and what that represents in terms of the ability of the agency to function.

Ms. WOODCOCK. Well, we really appreciate this, because CDER, when I took over CDER, first it was in 14 different locations scattered around the metropolitan area here. We expect a move this summer that will move the generic drug program to the White Oak campus, and also move the biologic therapeutics regulation, which has been located on the NIH campus, with their associated laboratories, to White Oak. And also our colleagues in the biologic center, with whom we work on policy very closely.

So for the drug center, this is a tremendous advance, will allow us both to have our new generic office on campus, as well as build our quality regulation organization, which I spoke about earlier, where we are going to have the same unit regulate pharmaceutical quality across all different types of drugs.

And also it will enable us to work with our colleagues at CBER very closely. And the benefits of having the device center right near us are tremendous, because there are many combination products with this new technology that is coming about that combine device elements and drug elements. So this has been a tremendous advance for us.

Mr. SHUREN. It has been a big deal for us as well. I would also put a plug in on personalized medicine. So much of it depends upon having the right diagnostics tied up with the therapeutics, and we work very closely with our colleagues in CDER. Having them down the hallway is essential.

And having the lab facilities to do absolutely critical work. And that is work that also helps companies. Getting product to market is so important. And one of the challenges we face in the current budget climate is we are getting to the point, getting very close to the point of starting to turn off lights in some of those labs.

Mr. SARBANES. Thank you very much. I yield back.

Mr. PITTS. The Chair thanks the gentleman.

Now recognize Mr. Guthrie 5 minutes.

Mr. GUTHRIE. Thank you. Thank you for coming. And this is a good hearing. And it is one of those things that when you run for Congress you don't think about these kind of issues. You have other things that you more readily read about. But when you get here, you realize they are vitally important to your constituents. We have people come continuously, and they are looking for devices, they are looking for approvals. And I think Mr. Shimkus talked about one specifically that is in a desperate situation. So it is important that we work together.

And I have a couple of questions. One is on the custom devices. And, Dr. Shuren, this would be for you. Those that are made by manufacturers for specific patients upon request by their physician

are critically important for patient care, but are not viewed by many as efficient or lucrative. And so therefore, in section 16 of the FDASIA, we established that manufacturers could modify an existing device for which data already existed instead of making an entirely new device.

The FDASIA language limits the manufacture or production of five units per year of a particular device type. And some in the industry have expressed concerns that the FDA may interpret this to say it can only be for five patients per year versus just five devices—only five patients who needed a custom device. And I think that might render that kind of ineffective. And so I just wonder how you interpret that provision.

Mr. SHUREN. No, we are not putting such a strict limitation on it. In the next few weeks we are going to put out draft guidance to try to better clarify implementation of that provision, which we think are very important provisions. And we support custom devices, and we think it is so helpful that Congress actually put in a much more clear standard for what is a custom device. And we are going to provide that clarity then in terms of interpreting it.

I would also add that companies do not need to come to us in order to go out with a custom device. There is no premarket review on it. They simply report to us annually. So hopefully in the next few weeks we will have out that guidance so we can have a fuller discussion with industry about it.

I will also say in those cases where they don't meet the statutory definition of a custom device, there are other mechanisms we have in place to help assure that patients who need a device that isn't otherwise approved on the market can get it. So many of those cases, even if the law doesn't allow a custom device, could be for compassionate use and still get it to the patient.

Mr. GUTHRIE. I know in the reporting that it makes it quicker and better for the patient. I guess there was some concern it might just be five patients. So in a couple weeks you are going to have that guidance, and if you could keep us informed, that would be fantastic.

I do want to point out that, I know we talked about sequestration, and we are dealing with budget issues here, and the budget conference committee is meeting as we speak through December, but the FDA has experienced a dramatic increase in appropriations over the past decade. And since the beginning of MDUFA, CDRH has gone from approximately 1,000 MDUFA full-time equivalents to over 1,400. And since 2004, CDRH has doubled its budget from 179 to 385. That is from 2004 to fiscal year 2011. And during this time PMA and 510(k) submissions have decreased.

However, studies have shown, and that is the CHI/BCG report we are all aware of, that review times have gotten 43 percent slower in the past few years and PMA 75 percent longer. So sequestration does have an effect, I am not saying that it doesn't, but there has been some substantial increase in the budget at the FDA as well.

So, Dr. Woodcock, one of the central tenets of the Prescription Drug User Fee program is to provide more certainty and predictability on the timeline for FDA to make decisions to approve a drug. And why is it important for companies in terms of continued

innovation and patient access to new medicines for companies to have predictability on the FDA and when it will make decisions on application?

Ms. WOODCOCK. Well, because these companies invest up to a billion dollars in a development program, and then they need to launch, and they have to do a lot of activities to get ready for launch. They have to get their facility all ready, distribution chain, all sorts of things. And so just knowing what the sequence of events is going to be and when that time on to market will be is extremely important to keep this enterprise afloat.

Mr. GUTHRIE. I agree with you. And then do companies receive patent term restoration based off the time it takes for a company to go through the FDA process?

Ms. WOODCOCK. Well, I don't understand this very well. They get restoration at the time of approval. So they get that. But there can be things eating away at their patent in the interim.

Mr. GUTHRIE. OK. And it is important, because our investment in research is second to none in the world. And I know, we talked in my office, Dr. Shuren, on some of the device companies that are going to other countries for better opportunities to get approval of their processes. And I appreciate the work that you have done on that, because we don't want to lose our industry and our leadership in research, and certainly not because of slow and unpredictable processes. So thanks for working to make that better.

And I yield back.

Mr. SHUREN. Thank you. If you may, Mr. Chairman.

Mr. GUTHRIE. I have three seconds. Go ahead.

Mr. SHUREN. And we are starting to see some changes. I just got called this week by a company who said we were actually going to conduct our first-in-human study overseas, and given the changes at the FDA they were going to start it in the U.S. And we are hearing that from other companies as well.

The numbers you gave in terms of our performance, they are from a report from 2010. And that is actually what I would say was the high point, the watershed mark for the program after about a decade of worsening. And since that time those numbers are actually down a fair bit. They are improving in review.

Mr. GUTHRIE. I understand. And I hope I didn't insinuate that. But I was just saying the funding has doubled since 2004. So there has been increased funding even though you are under sequestration now. So I just want to make that point.

Mr. PITTS. All right. The gentleman's time has expired. That concludes the first round of questionings. We will go to one follow-up per side.

Dr. Burgess, you are recognized for 5 minutes for a follow-up.

Mr. BURGESS. Thank you, Mr. Chairman.

Dr. Woodcock, can I just ask you briefly about the decision by the FDA to reschedule hydrocodone? Is there any update you can provide us on that?

Ms. WOODCOCK. Well, let me explain the process. What we do, we were asked, along with NIH, the National Institute for Drug Abuse, to provide a recommendation to HHS, who then provides a recommendation to DEA, who then go through a formal notification and comment process. And DEA actually does upscheduling. So

what we announced was simply the fact that we intended to recommend that the combination products be upscheduled.

Mr. BURGESS. Now, is there a report pending from FDA that we have not yet seen or has not yet been made public?

Ms. WOODCOCK. Correct. What we need to do to actually any scheduling action, we send something called an eight factor analysis, which is stipulated under the Controlled Substance Act, and findings based on that. And we write that up and send that to HHS, who then will evaluate it and then send recommendations to DEA. And that process, we should be moving that process along fairly soon. We expect to.

Mr. BURGESS. So we will have access to that report?

Ms. WOODCOCK. I don't know what point it becomes public. We can get back to you on that part of it.

[The information appears at the conclusion of the hearing.]

Mr. BURGESS. OK. Thank you. Well, you know, and it is a concern, there being practicing physicians all over the country who—sure, there are some things that require—State law requires triplicate prescription in Texas, those things can't be called in over the telephone in the middle of the night. But someone who has run out of a postoperative medication and still needs help, the doctor has the ability to get that help to that patient without an emergency room visit. So it is important, and it is something I don't want to see us lose.

We had a hearing here on, I guess it was on putting the EpiPen over the counter, an over-the-counter Epinephrine treatment for bee stings. And I don't remember now, quite honestly, who was here from the Food and Drug Administration that day, but I asked the question was there any thought to putting Narcan over the counter, Naloxone, so people would have the availability for that if they got into trouble abusing drugs that either they got legitimately or illegitimately. And then that was a feature of a story on Sanjay Gupta on CCN not too terribly long ago.

So where are we in that process? We have gone to great lengths to make levonorgestrel not just over the counter, but down there with the Snickers bars in the front of the pharmacy. Is there ever going to be any effort to make Narcan over the counter?

Ms. WOODCOCK. We are certainly encouraging development of forms of Naloxone. As you know, now it is compounded as nasal sprays and so forth and used by paramedics. So we are certainly encouraging development of sort of dosage forms that can be used out in the field under emergency situations. And then we would certainly consider whether over-the-counter access would meet the criteria for over the counter and then would improve emergency treatment of overdoses by friends and relatives, for example.

Mr. BURGESS. Well, thank you. Again, it was a pretty startling film clip that Dr. Gupta showed on that series, and again made me think again about the possibility that—again, no one wants to condone the use of illicit drugs, but on the other hand you hear about it where you lose—usually it is a teenager in our community and it is a terrible tragedy when it happens. And if there were another option maybe that would be a good thing.

Ms. WOODCOCK. We totally agree with you, and if lives could be saved that way then that is something we should really drive toward, and we are very aggressively pursuing this.

Mr. BURGESS. Don't misunderstand me, Mr. Chairman, it would be better if they never abused the compounds in the first place, but as a matter of first aid perhaps that is something should be considered. Thank you for the recognition. I will yield back.

Mr. PITTS. The Chair thanks the gentleman.

And now for follow-up, Mr. Sarbanes for 5 minutes.

Mr. SARBANES. Thank you, Mr. Chairman.

Dr. Shuren, I know when last year we were debating the various proposals around this reform one of the issues was where to draw the line, what the proper balance should be in terms of regulating medical devices. We wanted to make sure that, you know, on the one hand we had sufficient regulation in place and you had sufficient authority at the FDA to ensure that these devices are safe and effective and so forth. At the same time not have so much regulation that it becomes burdensome on industry to a point of sort of quashing innovation and investment.

And I would be curious generally for your thoughts on how industry has responded to where we kind of put that line where we struck the balance. And in particular I would be curious to hear you talk about the new, more streamlined process you have with respect to classification of devices from class 1 up to class 3, where I gather now you can use a kind of administrative process that doesn't necessarily involve full-blown rulemaking and comment, so forth, in every instance. And maybe you can give some examples of how you have used that authority in an effective way.

Mr. SHUREN. So, I mean, to answer the first part, I think after much discussion that occurred last time around FDASIA there was, I will say, general support for the U.S. standard of reasonable assurance of safety and effectiveness. And the question then becomes, what does that actually look like for particular kinds of devices?

What we have done is put in place this new benefit-risk strength work that is much more flexible and patient-centric to try to set the needle, if you will, in the right place.

One of the things that we are going to be following up in the coming months is to start talking about those circumstances under which data we might otherwise collect premarket can be shifted to the postmarket setting and not compromise patients, but do an appropriate reduction of burden on companies and address some of those cases in the postmarket setting. And that will include some new pathways for high-risk devices as well, and I think that is important.

Regarding classification, FDASIA provided some important changes to the process. One is the fact that we can now issue an order rather than a regulation. So in some respects it has gotten a little easier, and it has been helpful.

But let me tell you one wrinkle we have, and that is where if we do want to in fact reduce burdens on companies, appropriately so because with more experience we realize we should lower the classification, we should go from class 3 to class 2, or class 2 to class 1, we actually now have more steps to go through. We must hold an advisory committee meeting where before we didn't have to do

that. And that is actually making it more challenging for us under appropriate circumstances to reduce regulatory burden on companies.

Mr. SARBANES. Thanks very much.

Mr. PITTS. The Chair thanks the gentleman.

We have had a couple of members detained on the floor and missed the first round, so I will ask unanimous consent to recognize them as they come in for 5 minutes.

Dr. Gingrey, you are recognized for 5 minutes.

Mr. GINGREY. Mr. Chairman, thank you for that courtesy.

Dr. Shuren, the Office of Combination was created to deal with products that combine drugs, devices, or biologic products. For instance, some companies are toying with the idea of combining drugs and devices into solutions for antibiotic infections, something that I care about personally, as you know. However, the current approval method forcing companies with a mainly device product to go through a drug pathway because it induces a chemical reaction may discourage companies from investing in new and breakthrough technologies because the pathway is not best suited to what their product is.

The drug and device pathways were originally created decades ago when the reality of combination products were not yet realized. What steps is the FDA taking in light of its current 1970s framework to work directly with these companies who present the agency with 21st century technology like these combination products?

Mr. SHUREN. So the agency in setting up the Office of Combination Products, which sits in the Office of the Commissioner, is there to try to help determine what is the appropriate pathway for those combination products to go through. And they have been more recently trying to provide clarification for when the primary pathway would be device or drug.

But when it is a combination product there are needs that would be met for both, let's say, if it is a device and a drug, for the device side and for the drug side. So even if it is a product that we have primary responsibility for, if it has a biologic component, we go to our Center for Biologics for a consult. If it has a drug component we go to our Center for Drugs.

This is a very challenging area, I have to tell you this, because given the way the law is we have been able to try to minimize duplicative burden, if you will, and challenges on the postmarket side for reporting, or on good manufacturing processes, but when it comes to the standard for approving products the law right now is very challenging for combination product makers.

Mr. GINGREY. Dr. Shuren, thanks you very much.

Dr. Woodcock, the bipartisan GAIN Act took important steps to encourage the new development of antibiotics by focusing on incentives to new companies to keep companies in the marketplace. At this time can you provide me the number of qualified infectious disease products that have been designated since the law was passed last year, what, last year?

Ms. WOODCOCK. Certainly. We have designated, as far as I know, 27 products with 16 distinct active modalities. And that number will continue probably to increase.

Mr. GINGREY. Well, I really have to commend the FDA on that and realizing the desire and need for new antibiotics and acting quickly to implement the program. I have received plenty of positive feedback from companies, not just in my district, who have been able to achieve benefits through the GAIN Act.

I think you would agree with me that more needs to be done to combat resistance. One issue that needs attention involves susceptibility tests, interpretive criteria or breakpoints. Now, as you know, Dr. Woodcock, a breakpoint is criteria used to determine a particular infection's susceptibility or resistance to a specific antibiotic, and they are used by physicians in clinical decision making.

With the growing public health threat of antibiotic resistance, it is increasingly important to ensure that physicians have these tools they need to prescribe the right dose, of the right antibiotic, for the right patient, in the right situation.

Given what we know about the science behind breakpoints and our failure to keep pace with regulatory science in Europe, are U.S. patients receiving the best medical care, using the most up-to-date science, if the breakpoints for antibiotics are not accurate?

Ms. WOODCOCK. Well, they would not be. We have updated these criteria for about 121 of the 200 main antibiotic labels that exist. However, we feel that it would remain more up to date if we would not have this information remaining in the drug labels but rather would be able to point to a Web page and possibly to standard development organizations who are actually out there on the ground in the communities and are getting the information on an ongoing basis.

Even when we approve an antibiotic, we only look at a few organisms. As you well know, physicians have to use diagnostic criteria in the devices, the test for susceptibility, for a wide range of organisms, many of which may not be in any drug label. So we think we need a more dynamic and effective process that reflects the ongoing experience in the community.

Mr. GINGREY. Dr. Woodcock, I have about 2 seconds. I want to ask you to commit to me today to work with my office to fix the breakpoint issue, as well as look toward other ideas to address the epidemic of antibiotic resistance, one of the chief threats to public health today.

Ms. WOODCOCK. We would be delighted to do that.

Mr. GINGREY. Thanks, Dr. Woodcock.

And I yield back, Mr. Chairman. Thank you.

Mr. PITTS. The Chair thanks the gentleman.

That concludes the questions for the members. I am sure members will have follow-up questions. We would ask you to please respond promptly once you get them.

I remind members that they have 10 business days to submit questions for the record, and that means they should submit their questions by close of business on Tuesday, December 3rd.

A very informative hearing. Thank you very much, and thank you for your patience.

Without objection, the subcommittee is adjourned.

[Whereupon, at 12:17 p.m., the subcommittee was adjourned.]

[Material submitted for inclusion in the record follows:]

FRED UPTON, MICHIGAN
CHAIRMAN

HENRY A. WAXMAN, CALIFORNIA
RANKING MEMBER

ONE HUNDRED THIRTEENTH CONGRESS

Congress of the United States

House of Representatives

COMMITTEE ON ENERGY AND COMMERCE

2125 RAYBURN HOUSE OFFICE BUILDING
WASHINGTON, DC 20515–6115

Majority (202) 225–2927
Minority (202) 225–3641

December 17, 2013

Dr. Janet Woodcock
Director
Center for Drug Evaluation and Research
U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

Dear Dr. Woodcock:

Thank you for appearing before the Subcommittee on Health on Friday, November 15, 2013, to testify at the hearing entitled "Reviewing FDA's Implementation of FDASIA."

Pursuant to the Rules of the Committee on Energy and Commerce, the hearing record remains open for ten business days to permit Members to submit additional questions for the record, which are attached. The format of your responses to these questions should be as follows: (1) the name of the Member whose question you are addressing, (2) the complete text of the question you are addressing in bold, and (3) your answer to that question in plain text.

Also attached are Member requests made during the hearing. The format of your responses to these requests should follow the same format as your responses to the additional questions for the record.

To facilitate the printing of the hearing record, please respond to these questions and requests by the close of business on Thursday, January 9, 2014. Your responses should be mailed to Sydne Harwick, Legislative Clerk, Committee on Energy and Commerce, 2125 Rayburn House Office Building, Washington, D.C. 20515 and e-mailed in Word format to **Sydne.Harwick@mail.house.gov**.

Thank you again for your time and effort preparing and delivering testimony before the Subcommittee.

Sincerely,

Joseph R. Pitts
Chairman
Subcommittee on Health

cc: The Honorable Frank Pallone, Jr., Ranking Member, Subcommittee on Health

Attachments

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

The Honorable Joseph R. Pitts
Chairman
Subcommittee on Health
Committee on Energy and Commerce
House of Representatives
Washington, D.C. 20515-6115

SEP 09 2014

Dear Mr. Chairman:

Thank you for providing the Food and Drug Administration (FDA or the Agency) with the opportunity to testify at the November 15, 2013, hearing before the Subcommittee on Health, Committee on Energy and Commerce, entitled "Reviewing FDA's Implementation of FDASIA." This is a partial response for the record to questions posed by you and several other Committee Members to Dr. Janet Woodcock, in a letter we received on December 17, 2013.

Please let us know if you have any further questions.

Sincerely,

Thomas A. Kraus
Associate Commissioner
for Legislation

Enclosure

cc: The Honorable Frank Pallone, Jr.
Ranking Member
Subcommittee on Health
Committee on Energy and Commerce

We have restated your questions below in bold, followed by our responses.

The Honorable Joseph R. Pitts

1. **Congress enacted Title VIII of FDASIA, entitled "Generating Antibiotic Incentives Now (GAIN)," to provide incentives for the development of antibacterial and antifungal drugs for human use intended to treat serious and life threatening infections. Under GAIN, a drug may be designated as a qualified infectious disease product (QIDP) if it meets the criteria outlined in the statute. A drug that receives QIDP designation is eligible under the statute for fast track designation and priority review. According to section 505E(d)(l), the Secretary shall, not later than 60 days after the submission of a QIDP designation request, determine whether the drug is a qualified infectious disease product. The Committee understands that the Agency has not met the 60-day deadline on a number of submissions for QIDP designation.**

December 31, 2013, was used as a cut-off date for counting actions related to submissions for QIDP designation. As of December 31, 2013, the Agency had received 45 QIDP designation requests. Of those 45 requests, 41 were due on or before December 31. Of those, 32 (78 percent) were acted on within 60 days. As discussed in more detail in response to Question 2 below, most delays have been due to complex legal, scientific, and policy questions that needed to be addressed in the context of particular requests for QIDP designation.

2. **Is there presently a backlog of pending QIDP submissions at the Agency? What percent of QIDP designations has the Agency acted on timely? As of September 30, 2013, how many sponsor submissions for QIDP designation were beyond the 60-day review period? And how many determinations, if any, has the Agency made since October 16, 2013? Is there presently a legal or policy issue under review within the Agency regarding QIDP designations?**

As of December 31, 2013, the Agency had received 45 QIDP designation requests. Of those 45 requests, 41 were due on or before December 31. Of those, 32 (78 percent) were acted on within 60 days. Most delays have been due to complex legal, scientific, and policy questions that needed to be addressed in the context of particular requests for QIDP designation. As of September 30, 2013, three requests were pending beyond their 60-day review period. Two other QIDP requests that were acted upon prior to September 30, 2013, were overdue at the time of action. Eight determinations were made between October 16 and December 31, 2013. As with any new legislation, there have been a number of legal and policy issues that had to be considered since the enactment of FDASIA. However, there are currently no issues that need to be resolved associated with any pending QIDP request.

3. **Congress is concerned that certain agency interpretations of the GAIN Act may inadvertently limit the development incentives Congress enacted. For example, we have heard that the agency may be designating QIDP status for a drug in a specific indication, rather than for a drug itself, and that the provisions of21 U.S.C. 355f(c) "Limitations" may be interpreted in a way that renders 5-year exclusivity extension unavailable if a**

sponsor initially seeks approval for a different indication. Requiring a particular sequencing of indications creates hurdles that could reduce the incentives to develop the drug, even once a drug has received QIDP status and therefore has been deemed to be intended to treat serious or life threatening conditions. Please explain how FDA has interpreted the statutory exclusivity to apply if a drug receives QIDP designation, but then receives a first NDA approval for a different indication than the one described in the QIDP application.

We believe that the Agency's implementation of the GAIN Act has been consistent with Congress' intended goal to encourage the development of antibacterial and antifungal drugs that treat pathogens that cause serious or life-threatening infections. Indeed, as of December 31, 2013, FDA has granted 35 QIDP designations. FDA believes the number of QIDP designations granted indicates that the Agency's interpretation of the GAIN provisions have not limited the development incentives intended by Congress.

As of December 2013, the Agency has not yet approved a new drug application (NDA) or made an exclusivity determination for a drug that has received QIDP designation. Since that time, the Agency has approved two drugs that were designated as QIDPs. However, because both of these drugs were new chemical entities and were approved for the indications for which they had received QIDP designation, we have not yet interpreted and applied the provisions of 355f(c) ("Limitations").

4. **Does FDA interpret 21 U.S.C. 360n-1 and 356(a)(l) (as amended by the GAIN Act) to require the Agency to mandatorily apply fast track and priority review procedures, or only if an application for a product with QIDP status requests these review timelines and procedures? Does FDA regard this issue as impacting the availability of exclusivity in any way?**

FDA determines whether an application qualifies for priority review (versus standard review) for every application, not just when requested by the applicant. Therefore, the Agency will grant priority review to an application for a QIDP, regardless of whether the sponsor requests priority review status. However, while the GAIN Act guarantees that a product receiving a QIDP designation automatically qualifies for fast track designation, 21 U.S.C. 356(a)(1) states that fast track is granted "at the request of the sponsor of a drug." This request can be made with the QIDP designation request, or at any time during drug development, and can be quite simple (e.g., "Company X requests designations of QIDP and fast-track status for..."). No additional justification by the sponsor is needed to support the fast track designation of a drug that is granted a QIDP designation. The Agency does not believe this issue will impact the availability of exclusivity.

5. **To further oversight and reassessment of QIDP incentives within 5 years after the enactment of GAIN, the Secretary of Health and Human Services must submit certain program information to the House Energy and Commerce and Senate HELP Committees, including, for example, a list of qualified infectious disease products and information on the types of exclusivity granted for each product, along with other product information. Does FDA intend to limit the disclosed information in accordance with existing protections of the Freedom of Information Act and other applicable laws? For example,**

will information about unapproved applications be disclosed or protected from disclosure?

FDA intends to limit the disclosed information in accordance with existing protections of the Freedom of Information Act and other applicable laws and regulations. Specific information about unapproved applications will not be disclosed.

6. **The Committee would like to thank the FDA for its outstanding work to address the public health crisis of unintentional overdoes of acetaminophen. Recognizing the high incidence of liver damage due to acetaminophen overdosing, the Agency has responded with a variety of measures to improve safety, including developing education programs and improving the labeling of acetaminophen-containing products. However, one aspect of the Agency's response still concerns me and that is the removal of prescription combination products containing acetaminophen in quantities greater than 325 mg by January 14, 2014.**

   So that we can continue to protect the health of U.S. citizens from the unintentional overdoses of acetaminophen, please provide a response to the following questions:

   a. **What are the plans of the FDA to enforce the January 14, 2014, deadline and ensure that no prescription products containing no more than 325 mg of acetaminophen remain on the market after that date?**

   FDA received voluntary requests for withdrawal from all but six of the affected holders of Abbreviated New Drug Applications (ANDAs) for prescription combination drug products containing more than 325 mg acetaminophen per dosage unit. This comprised 108 individual ANDAs. Those products were listed in a *Federal Register* Notice that immediately withdrew approval of those applications upon its publication on May 1, 2014.

   On May 1, 2014, FDA also announced its intention to withdraw approval of the ANDAs for the six remaining sponsors that did not voluntarily withdraw approval via a Notice and Opportunity for a Hearing (NOOH). All of those sponsors had already stopped marketing their products. None of the ANDA holders listed in the NOOH requested a hearing, and FDA intends to issue a notice withdrawing approval of their ANDAs shortly. Upon publication of that notice in the *Federal Register*, there will no longer be any approved prescription combination drug products containing more than 325 mg acetaminophen per dosage unit.

   b. **Does the FDA intend to do a full and total recall on January 14, 2014, including one that has pharmacies removing these products from inventory for sale? If not, what steps is the FDA taking today to ensure that manufacturers have stopped production, distributors have slowed distribution, wholesalers have scaled back inventory, and pharmacies are allowing current stock of the high dose products to run out and are prepared to transition to the new products on January 14, 2014?**

Please see our answer to Question 6a above, regarding withdrawal of approval or prescription combination drug products containing more than 325 mg acetaminophen per dosage unit. In addition, FDA issued multiple statements and reminders to health care providers to stop prescribing prescription drug combination products that contain more than 325 mg of acetaminophen per dosage unit. In addition, we recommended that pharmacists stop dispensing those products, and that when a pharmacist receives a prescription for a product containing more than 325 mg of acetaminophen per dosage unit, they contact the prescriber to discuss a product with a lower dose of acetaminophen.

c. If a full and total recall on January 14, 2014, is not the intention of the FDA, are you going to share with the industry and the public the rationale for that decision, in light of the safety concerns that prompted the original request in January 2011?

As noted in our responses to Question 6a above, FDA has initiated, and is close to completing, the necessary regulatory steps to withdraw approval of all ANDAs for prescription combination drug products containing more than 325 mg acetaminophen per dosage unit.

Consistent with the Agency's authority, we often implement safety withdrawals by requesting that sponsors voluntarily withdraw the product from the market. Subsequent regulatory steps are then undertaken to formally withdraw the applications for the products that were not voluntarily withdrawn and to make a determination that they have been withdrawn for reasons of safety. In the case of prescription combination drug products containing acetaminophen, given the large number of applications and various regulatory considerations (such as the fact that the subject drugs are "scheduled" and subject to Drug Enforcement Administration (DEA) quotas), we used a public notice with ample lead time to initiate this action.

Generally, we only request withdrawal of a product from the patient or pharmacy level where there is a risk of imminent harm to the patient. The intent of this effort was to reduce the amount of acetaminophen to 325 mg per dosage unit so as to lessen the overall exposure of patients to acetaminophen and thereby diminish the potential for exceeding the toxic threshold of the drug that could cause liver injury. The Agency has not identified an imminent hazard associated with the use of the product by individual patients that would warrant immediate removal of these products at the patient level.

Finally, we believe that by telling health care providers to stop prescribing combination drug products that contain more than 325 mg of acetaminophen per dosage unit and pharmacists to stop dispensing those products, the products will leave the market in an efficient manner, and that this exit also will be sufficiently gradual so as not to disrupt clinical practice or create shortages of these important drugs.

d. Does the FDA have an early indication of whether all pharmaceutical manufacturers intend to meet the FDA's request that all prescription products with more than 325 mg of acetaminophen be withdrawn from the market by January 14, 2014?

Yes. As noted in our response to Question 6a above, as of January 14, 2014, all but six of the affected ANDA holders voluntarily withdrew their products from the market. The remaining six sponsors had already discontinued marketing their products, but did not adequately respond to the January 2011 *Federal Register* notice. Therefore, those sponsors were notified via a NOOH that approval of their applications was going to be withdrawn. Because none of them requested a hearing, FDA proceeded with the necessary regulatory steps to withdraw approval of their applications.

7. **How does the FDA work with DEA after they have reviewed an application and made a scheduling recommendation? Is the DEAs scheduling review process incorporated into the PDUFA timeline? What could be done to improve the DEA scheduling process from the FDA's perspective?**

Generally, after DEA receives a scheduling recommendation from the Department of Health and Human Services (HHS) and prior to DEA's publication of the Notice of Proposed Rule Making (NPRM), FDA staff are available to provide clarifying information to any questions about the recommendation that DEA may need answered. The DEA scheduling review process is not incorporated into the PDUFA timeline, because scheduling of a drug falls under the Controlled Substances Act, which DEA administers, and not the Federal Food, Drug, and Cosmetic Act (FD&C Act), under which drugs are approved by FDA. While FDA understands how important it is to make sure the scheduling process is efficient and timely, we do not have enough knowledge of the DEA internal review processes to make any comments on ways to improve them. FDA has focused our efforts on improving our internal processes, with a goal of preparing a scientifically rigorous recommendation for HHS to transmit to DEA as quickly as possible.

8. **One of the anecdotes we hear from industry and investors, and the data seem to support, is that for certain therapeutic areas, such as oncology, the FDA has an exceptional track record of rigorous but efficient and timely review process, but for others it is long and drawn out. FDASIA requires some very basic review-level data and provides an opportunity for further analysis to enhance our understanding by looking at review times and other metrics by review division. Recognizing differences in science and disease understanding, what are you doing to replicate some of the best practices in your strongest review divisions across the agency?**

CDER developed a standardized review model that applies to the review of all new drugs and biologics applications. The model is called "21st Century Review" and has been applied to all applications across all review divisions, starting in FY 2009. CDER staff has received extensive training on this new review model, which was designed to ensure consistent application of best practices across all review divisions. Implementation of the new review model has been very successful and served to lay the groundwork for implementation of the "Program" for review of new molecular entity NDAs and new BLAs that is a new performance goal under PDUFA V. Of note, CDER's Office of Hematology and Oncology Products (OHOP) has established a commendable track record in expediting the review of promising new drugs for patients with cancer. The same principles and best practices utilized in OHOP are also applied in other divisions and offices to expedite the review and approval of promising new drugs that treat serious and life-threatening diseases in patients with unmet medical need. For example, a new drug that treats the underlying cause of cystic fibrosis in some patients with that rare genetic disease was approved in

January 2012 by the Division of Pulmonary, Allergy, and Rheumatology Products, several months ahead of the PDFUA goal date.

In addition, under the new Breakthrough Therapy (BT) program that was part of FDASIA, FDA has made an institutional commitment to work closely with sponsors to expedite the development and approval of new drugs for serious and life-threatening diseases that may provide a substantial improvement over existing therapies. This commitment includes involvement of senior FDA leadership in the review process. While almost half of the BT designations granted by FDA to date have been for drugs intended to treat hematologic and oncologic diseases, many other CDER review divisions have also granted BT designations and are committed to supporting the goals of the program, including utilizing all the available tools to expedite development and approval of these promising new drugs.

10. Since GDUFA does not provide review of predictability or metrics for backlog ANDAs or for ANDAs submitted during the first two years of GDUFA it is difficult to quantify the work the Agency has been doing. What has the FDA done to improve communication with industry in order for manufacturers to be able to predict when the FDA might take action on these applications?

FDA appreciates industry's need for predictability and has been collaborating with the Generic Pharmaceutical Association (GPhA) for the past several months to develop improvements in this regard. We have taken several steps in response to industry's concerns.

For example, FDA has begun to issue Complete Response (CR) letters to generic drug applicants. These CR letters outline deficiencies found after completion of an application review from all review disciplines (with or without inspection). These and Easily-Correctable Deficiency (ECD) letters convey deficiencies found during the review of an application.

FDA has also initiated assigning internal goal dates to applications to proactively align the application review with the goal due dates scheduled to be implemented in year three of GDUFA. We will inform industry about when to expect Agency action on specific applications.

In addition, FDA's Center for Drug Evaluation and Research (CDER) is developing a systematic process to provide meaningful status updates and also predict the likely timing of action on pending work. As an early step in this process, FDA published a Manual of Policies and Procedures (MAPP)[1] which, among other items, designates the Regulatory Project Manager as the primary point of contact for all inquiries on ANDA status. This policy is consistent with FDA practices in other Centers and other User Fee Programs. Designating one point of contact ensures centralized and streamlined communication flow, good communication practices, consistency in information provided, and appropriate documentation of communication. The Agency is also working on a MAPP to provide clarity and predictability regarding prioritization of different types of submissions, including those in the backlog and those submitted during Years 1 and 2 of GDUFA. We have been consulting with industry regarding prioritization.

Our goal is to address these issues systematically, rather than on a case-by-case basis. Prior to GDUFA, industry representatives placed a high volume of informal status inquiries to FDA

[1] See MAPP 5020.1: Responding to Industry Inquiries with respect to Abbreviated New Drug Applications in the Office of Generic Drugs.

reviewers, supervisors, and senior staff, and informally advocated to expedite review of the most commercially significant submissions. FDA responded to these inquiries on an ad hoc basis. This practice was highly resource-intensive and often inadequately documented. It could also result in differential treatment of similarly situated applicants, giving rise to fairness and consistency concerns.

Many of the steps we are taking to improve communications go above and beyond our negotiated GDUFA commitments, and constitute an extra effort to ease the generic drug industry's transition into a user fee environment for the first time. We welcome the opportunity to brief your staff on these improvements.

11. Of the 234 new hires under GDUFA, will you breakdown approximately how many hires were on-board in each of Q 1, Q2, Q3 and Q4 of FY 20 13? Are all 234 new hires actually on-board today? New hires is an important foundational goal of GDUFA, and actually one of the only goals for FY 2013 and FY 2014. Will you further explain why it took so long for the FDA to actually hire and on-board the 234 FTEs?

FDA agrees that hiring new employees under GDUFA is an important foundational goal. As such, coordination within the Agency was essential in order to properly identify the necessary positions to meet the business needs for the generic drugs program. Numerous rounds of vetting and prioritization also took place to ensure that the Agency was properly prepared for these new hires. Additionally, to address the large number of similar positions, a corporate recruitment approach similar to that of the National Institutes of Health was developed to increase overall efficiency.

FDA is pleased to note that as of December 2013, almost all 234 new hires were on board. Recruitment efforts continue to bring new hires on board.

Hiring by Quarters for FY 2013:
Quarter 1 – 62
Quarter 2 – 25
Quarter 3 – 87
Quarter 4 – 60

12. We recognize training is vital for new hires. Approximately how long does it take a new FDA Employee to become a fully productive ANDA reviewer or facility inspector?

The length of time until a new reviewer or facility inspector becomes fully productive is dependent upon their experience level. With new hires of limited experience, it generally takes approximately two years for the new hire to reach this point. As part of the initial hiring strategy, FDA targeted recruitment and has hired staff with experience to shorten this time frame. For example, many of our new chemistry reviewers arrived at FDA with previous pharmaceutical industry experience, which should shorten the time it will take for them to be fully productive.

13. Given the backlog of pending ANDAs and facility inspections (the tenets or principles on which GDUFA was negotiated, legislated and implemented), will you give the Committee an estimate on how many of these new hires are scientists dedicated to ANDA review? How many are to be facility inspections? And of the remaining 234 not accounted for in

these two principle job functions, what job functions will they be providing related to GDUFA?

As of December 2013, an estimated 98 positions are dedicated to ANDA review. An estimated 80 positions in the Office of Regulatory Affairs are dedicated to facility inspections. The majority of the remaining positions will provide support in the form of information technology and administrative duties. Information technology support for the generics program will include the building of new IT systems, such as the one needed to track and monitor review times, as well as a billing system. Administrative positions will be dedicated to offer program support infrastructure, including staff, to bring on and train the new hires.

14. **For FY14, you have a goal of approximately 465 new hires. Please provide the breakdown by Quarter in FY 14 for on-boarding these new hires and the functional areas they are to be assigned.**

    Despite the slow start, I commend the FDA for being able to fill so many positions in the latter half of FY 13. Does the rapid hiring at the end of FY 13 mean that the FDA now has a well- established hiring process for the GDUFA program and will be able to meet this hiring goal earlier in the year for FY14? For example, it is my understanding that GDUFA is estimated to support the hiring of about 900 new FDA employees by the end of FY 15. How many of those new hires will be dedicated to actual technical review of pending ANDAs and inspectional review of facilities, as opposed to administrative functions within CDER?

As of August 2014, FDA has on-boarded 447 GDUFA hires, reaching 96% of the goal for FY2014. Approximately an additional 167 positions are pending. The FY2014 quarterly breakdown is as follows:

FY 2014 Breakdown of GDUFA Hires	
Quarter 1	90
Quarter 2	112
Quarter 3	185
Quarter 4 (as of August 2014)	60
TOTAL	447

The functional areas that the GDUFA hires support are review, inspection, administration and program support.

The Agency has an established hiring process. The Corporate Recruiting Process we have adopted allows FDA to announce positions for 120 days to fulfill multiple hiring demands for similar positions. This eliminates the need to create multiple and repetitive vacancy announcements. It also allows hiring managers to receive certificates of eligible candidates every 30 days without the delay of repeating the job announcement process. Further, the Agency continues to actively engage in outreach efforts to attract and identify potential candidates. FY 2013 had 98 of 234 positions dedicated to ANDA review, or 42 percent. In keeping with a similar average, we estimate that for FY 2014, there should be 187 new reviewer positions in the Office of Generic Drugs, or 40 percent of the 465 positions needed. We estimate that for FY 2015, the remaining 222 positions will be

added to equal the Agency goal of 921. Staying consistent to the previous years, 40 percent for FY 2015 would be 89 new hires dedicated to ANDA review.

15. Over the past several years, the U.S. Food and Drug Administration (FDA) has been tasked with the evaluation and the weighing of the appropriate use of opioid analgesic drug products. For the millions of American patients experiencing an acute medical need or living with chronic pain, opioids, when prescribed appropriately, can allow patients to manage their pain as well as significantly improve their quality of life.

At the same time, this Committee has become increasingly concerned about the abuse and misuse of opioid products, which have reached epidemic proportions in certain parts of the United States. The value of, and access to, these drugs for patients in pain is unquestioned. My concern is that the FDA has yet to establish nor has yet determined how to balance the need to ensure continued access to those patients who rely on continuous pain relief while addressing the ongoing concerns about abuse and misuse.

Abuse Deterrent Formulations (ADFs) for scheduled narcotics show significant promise to reduce prescription drug abuse. While not yet perfect, even the FDA has recognized that the ADF technology as applied to the recently approved reformulation of OxyContin is a significant step in protecting patient's access while curbing abuse of this powerful opioid.

With the foregoing in mind:

a. When does the agency expect to finalize its draft labeling guidance?

FDA shares your concerns regarding prescription drug abuse, including the abuse of opioid analgesics. We are strongly committed to finding ways to reduce abuse and misuse of these medications. The draft guidance addresses both the evaluation and labeling of abuse-deterrent opioids. We intend to finalize the guidance as soon as possible. The evaluation of abuse-deterrent formulations (ADFs) is a new and evolving area of scientific and regulatory investigation, and FDA recently participated in a scientific meeting to hear comments about issues pertaining to ADFs. In addition, FDA is directly supporting research into ADFs, both through the conduct of research in FDA laboratories and also by supporting independent scientific research at Purdue University and the University of Maryland. FDA is also working with the manufacturers as they develop new ways to prevent misuse and abuse. FDA believes that these new approaches are important to understand, and we are doing what we can to support their development and use.

b. Will you consider the approach outlined in the draft labeling guidance to be equally applicable to products other than opioids?

At the present time, we are focusing our policies on the opioid drug products. Certain other categories of prescription drug products, such as stimulants used for Attention-Deficit/Hyperactivity Disorder, are also subject to misuse and abuse. However, the draft guidance is focused on opioids, as their patterns of abuse are different from those of non-opioid drugs, and the abuse of opioids poses a greater public health risk.

c. Does FDA believe that it has sufficient existing authority to incentivize development of abuse deterrent products?

FDA understands the importance of finding ways to reward the development of successful ADFs (for example, by approving labeling, which includes accurate descriptions of a product's abuse-deterrent properties). For example, applications for abuse-deterrent products generally will be eligible for fast track and priority review. The FD&C Act also provides for certain periods of marketing exclusivity, if the applicable criteria are met.

If FDA concludes that an extended-release/long-acting (ER/LA) opioid drug product has abuse-deterrent properties, the Agency has authority under current law to require a generic version of that product to also have abuse-deterrent properties.

d. If so, will the FDA utilize all of its existing authorities to create incentives for such products?

FDA continues to work to encourage the development of ADFs of opioids through a variety of actions, including meetings with sponsors, guidance, and accelerated reviews, wherever appropriate.

e. Why did the FDA approve a new product, Zohydro, without requiring an ADF in the formulation? Can Zohydro in its approved form be crushed and snorted or crushed diluted and injected?

FDA approved Zohydro ER after concluding that its benefits outweigh its risks, notwithstanding the fact that the product does not have abuse-deterrent properties. We approved this product because it offers a new option for the management of pain severe enough to require daily, around-the-clock, long-term treatment and for which alternative treatment options may be inadequate. In addition, as a single-entity hydrocodone product, it is not associated with the liver toxicity risk of the combination hydrocodone products that include acetaminophen. Zohydro ER is the first opioid to have strengthened labeling to help prescribers identify the select group of patients for whom it could be beneficial. Like all opioids, Zohydro ER has the potential for misuse and abuse, and the strengthened labeling also warns prescribers and patients about the risks of Zohydro ER and strongly recommends careful monitoring to reduce the risks of misuse and abuse. FDA takes the safety of Zohydro ER and all opioids very seriously and will actively monitor their utilization to identify any emerging issues.

All opioids are subject to abuse, including those that have abuse-deterrent properties. We expect that some people intent on abusing these drugs will be able to circumvent many of the abuse-deterrent formulations currently on the market or in development. In addition, no products or technologies have yet proven successful at deterring oral abuse—the most common form of opioid analgesic abuse. As noted previously, FDA believes the new warnings and education for prescribers and patients will help support appropriate prescribing and follow up for patients.

f. Does the FDA believe that there will be an expanded use of ADFs without an Agency mandate to include such formulations in new NDAs/ ANDAs?

We believe that there are ways to expand the development and use of ADFs using our existing authorities. FDA is actively discussing and supporting the development of ADFs when manufacturers meet with the Agency to discuss development of new products. In those meetings, FDA reinforces our goals to encourage the development of robust and successful ADFs for opioids, wherever possible. In addition, as discussed above, FDA anticipates that appropriately describing a product's abuse-deterrent properties in approved labeling will assist prescribers and payers in making decisions about which products to use and increase the use of products with ADFs.

16. In January, the FDA issued a draft guidance for industry on development and labeling for abuse deterrent formulation ("ADF") products. Although the draft guidance lists the basic concepts of FDAs perspective on ADFs, from technology manufacturers the paper lacks both clarity and detail necessary to support the development and broad application of ADF technology for abused products. For example,

a. Some of the references and examples made in the guidance are applicable to only a subset of technology approaches and not relevant to others.

The scientific and regulatory concepts set forth in the draft guidance should be applicable to a wide range of technologies in addition to those discussed directly in the document. Recognizing that the technologies being used are all different, the intent of the Guidance is to provide a framework about the types of non-clinical and clinical studies that we believe will be most useful in assessing ADFs, as well as how FDA will assess these studies and include them, when appropriate, into labeling.

b. There is no detailed guidance on differential requirements for immediate release opioids and combination products.

Given the higher public health risk posed by ER/LA opioids as a result of the higher amounts of opioids in each dose, the focus of FDA has been on the development of ADFs for these products. However, many of the scientific and regulatory concepts set forth in the draft guidance will be applicable to immediate release (IR) products. Also, the evaluation and labeling of combination products (such as an opioid agonist and antagonist combined in a single product, e.g., morphine sulfate/naltrexone) are discussed explicitly in several sections of the draft guidance document.

c. A perspective on how to address newly introduced ADF products that do not have a non-ADF predecessor version or reference product is missing.

The development of an ADF product that lacks a non-ADF predecessor is not discussed specifically in the draft guidance, but we believe the scientific and regulatory concepts discussed in the draft guidance document may be applicable to such development programs. As discussed in the draft guidance, FDA will take a flexible, adaptive approach to the evaluation and labeling of potentially abuse-deterrent products. FDA will evaluate each potential ADF on a case-by-case basis and work with the sponsors of novel products to

provide product-specific advice. For example, we believe that non-clinical and human studies comparing the new ADF formulation to the drug substance can help to predict the effect of the ADF on abuse. When the data predict or show that a product's potentially abuse-deterrent properties can be expected to—or actually do—result in a meaningful reduction in that product's abuse potential, FDA will approve inclusion of these data, together with an accurate characterization of what the data mean, in product labeling.

d. Last, there is not any structured guidance on how FDA is going to assess ANDA applications in the context of the guidance requirements.

FDA is currently developing guidance on the approach we intend to take when assessing generic forms of opioids when there are approved innovators that are demonstrated to be abuse-deterrent, and that guidance will be published in draft form as soon as possible.

Although technology developers and manufacturers started developing ADF technologies more than ten years ago, the FDA claims that the science of abuse deterrent formulation assessment is new and requires case-by-case assessment. This position lacks the clarity and reliability necessary for companies that require continuous funding and investment for their technology development.

Will you give this Committee a specific date by when the FDA will finalize the guidance for ADF development labeling, including addressing the missing pieces I just mentioned?

We intend to finalize the guidance as soon as possible.

17. Do you believe that FDA is lacking legislative authority to reject approval for non-ADF extended release opioid products?

Please see responses to Question 15e and f (above).

18. Does the FDA believe it should be able to continually progress the opioid market into one where all opioids will have to have ADF technology to protect and minimize misuse and abuse?

FDA strongly supports the development and broader use of effective opioids with abuse-deterrent properties. As explained in previous responses, however, we do not believe it is feasible or appropriate to require all products in the class to have abuse-deterrent properties, at this time. In light of the need for further data and scientific development in this nascent and rapidly evolving area, FDA intends to continue to take a product-by-product approach to regulatory decisions concerning the safety and effectiveness of opioid products.

23. Please provide the Agency's Social Media budget and strategy plan to the Committee.

FDA strives to present clear, accurate, timely, and relevant information to Americans in the same online spaces as many other purveyors of health and safety information. To do this effectively, we proactively embrace new technologies on an ongoing basis. As a public health and regulatory agency, FDA must provide the public with clear, concise, and accurate information on a wide range of important public health initiatives. In doing so, the Agency uses multiple communication

channels, including social media. FDA encourages the use of social media technologies to enhance communication, collaboration, and information exchange in support of our mission to protect and promote public health. Expanding our external interactions increases the potential for our stakeholders to gain a better understanding of the work and actions that the Agency takes regarding all FDA-regulated products.

For example, FDA uses Twitter regularly to distribute information on product approvals, Warning Letters, recalls, policy announcements and other relevant information. More than 800,000 followers have signed up to receive these tweets, many of which are forwarded, extending their reach to millions. FDA posts similar information to its Facebook page, which is tracked by nearly 95,000 people.

With regard to budget, there is no specific dollar amount allotted to social media within FDA; rather, social media is incorporated into the communication budgets of FDA's Office of External Affairs (OEA) and the various FDA centers.

OEA is responsible for setting the Agency-wide social media strategy as well as ensuring its governance. OEA is currently in the process of developing a strategy to optimize the use of social media in order to further the Agency's mission.

24. It has been the agency's policy and practice that in vivo (human) clinical testing is required to establish bioequivalence for most locally acting topical drugs. What scientific determination did FDA make to justify its departure from this prior policy and practice when it issued its new draft biocquivalence guidance for cyclosporine ophthalmic emulsions?

Under FDA's regulations, bioequivalence (BE) may be demonstrated by several in vivo and in vitro methods. The selection of a specific method used to establish BE will depend upon the purpose of the study, analytical methods available, and the nature of the drug product. FDA issues product-specific guidance documents that set forth recommended approaches for establishing BD for specific drugs.

On June 20, 2013, FDA published a *Federal Register* notice announcing the availability of draft guidance for industry, containing BE recommendations for cyclosporine ophthalmic emulsion. The draft BE guidance addresses two methods for BE studies, an in vitro method and an in vivo method.

The draft guidance recommends that an in vitro method may be used when the proposed generic drug and the reference listed drug (RLD) formulations are qualitatively and quantitatively the same, with respect to active and inactive ingredients. The draft guidance further provides that an in vivo method, i.e., a BE study with clinical endpoints, for cyclosporine ophthalmic emulsion, is requested when the generic drug has a different inactive ingredient, a difference of more than 5 percent in the amount of any inactive ingredient compared to that of the RLD, or unacceptable data from in vitro comparative studies.

FDA opened a public docket to collect comments on the draft guidance from industry, stakeholders, and the general public. FDA will carefully consider all submitted comments on the draft BE guidance for cyclosporine ophthalmic emulsion.

26. The Federal Food, Drug, and Cosmetic Act (Act) stipulates that the critical distinction between a drug and a medical device is that a medical device "does not achieve its primary intended purpose through chemical action within or on the body of man." The plain language of the Act indicates that a device may have more than one primary intended purpose. In 2011, however, FDA issued a draft guidance titled "Classification of Products as Drugs and Devices & Additional Product Classification Issues" indicating that if a product has "multiple therapeutic effects," each would be considered a "primary intended purpose." By designating all purposes as primary, this statement appears to be inconsistent with the plain language of the Act. The draft guidance also states that if any of these intended purposes were achieved through a chemical action within or on the body of a man, the product would not meet the definition of a medical device. This change in policy has resulted in products that would have been historically regulated in the U.S. as devices being regulated as devices in the rest of the world, but regulated as drugs in the United States. I have several questions regarding this draft guidance and how FDA is classifying medical devices:

a. Given that there are numerous products classified as devices that have some chemical action within or on the body of man, would you agree that the draft guidance reflects a substantial policy change by requiring a product to be classified as a drug if any of its intended purposes are achieved through a chemical action within or on the body of a man?

As you note, FDA issued the Draft Guidance on "Classification of Products as Drugs and Devices and Additional Product Classification Issues"[2] and related Draft Guidance on "Interpretation of the Term Chemical Action in the Definition of Device under Section 201(h) of the Federal Food, Drug, and Cosmetic Act"[3] in 2011. These draft guidance documents concern classification of products as drugs and devices. The Agency is currently working to finalize these draft guidance documents.

The Agency does not interpret the statutory definition of device in section 201(h) of the FD&C Act, 21 U.S.C. § 321(h), to exclude all products that exhibit chemical action within or on the body of man. A product that exhibits chemical action within or on the body of man may meet the device definition, provided that the product "does not achieve its primary intended purposes through" such chemical action. Thus, for example, if a product's chemical action contributes to an effect other than a primary intended purpose of the product, the product could fall within the scope of the device definition.

b. Would you agree that similar products should be regulated in the same manner and that the substantial policy change could have an impact on new products being regulated similarly to products on the market prior to issuance of the draft guidance?

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[2] Available at *http://www.fda.gov/RegulatoryInformation/Guidances/ucm258946.htm.*
[3] Available at *http://www.fda.gov/RegulatoryInformation/Guidances/ucm259059.htm.*

FDA strives to regulate similar products in a similar manner. Further, as explained in the draft guidance documents referred to in the response to Question a. (above), FDA classifies products in accordance with the statutory definitions established by Congress. Differences in product composition or intended uses, or both, can affect product classification. Due to such factors, products that appear to be similar may, in fact, not be similar and, thus, have different classifications.

Finalizing the above-referenced draft guidance documents will help regulated entities understand what factors affect product classification so that they can make informed judgments regarding how their products would be classified and what questions they may wish to address with the Agency. It is an important initiative to the Agency to enhance predictability and transparency for industry.

c. The plain language of the Act indicates that a device may have more than one primary purpose. The 2011 FDA draft guidance appears to arbitrarily depart from this plain language. What is the rationale for doing so?

We agree that a device may have more than one primary intended purpose. We intend to make this point clear in the final guidance.

d. This draft guidance has not been finalized but appears to have been implemented by FDA. Would you agree that a draft guidance document should not be implemented until final?

FDA must implement its statutes and regulations, regardless of whether it chooses to issue guidance in an effort to provide greater detail and transparency to industry and other stakeholders. The draft guidance documents referred to in the response to Question a. (above) are meant simply to provide more detail regarding FDA's implementation of its existing statutory and regulatory obligations. Indeed, the process for classifying a product as a drug, device, biological product, or combination product in response to a request for designation has a 60-day time limit for issuing a decision (*see* 21 U.S.C. § 360bbb-2). Therefore, FDA applies current interpretations of the applicable statute and regulations, including applicable case law, to engage in case-by-case decisions on requests for designation within the statutorily mandated time period. FDA also follows its regulations at 21 CFR 10.115 in developing guidance documents.

e. The FDA recently applied its revised interpretation of the Act set out in the 2011 draft guidance to classify a portable body shower as a drug rather than a medical device. The U.S. District Court for the District of Columbia found that the FDA designation of the product as a drug was based on a "doubly grandiose" interpretation of the phrase "primary intended purpose." When and how will FDA revise the 2011 draft guidance to reflect the ruling?

The product to which you refer—Diphoterine Skin Wash—is not a "portable body shower." It is comprised of a pressurized canister that delivers a diphoterine solution onto the skin as an aerosolized mist. It is intended to help prevent or minimize accidental chemical burn injuries. The diphoterine solution is expected to react with harmful chemicals to neutralize

them, draw chemicals from the interior to the exterior of the skin, and displace chemicals from the body. The device canister aids in delivery of the diphoterine solution by allowing its ready delivery onto the skin. FDA classified the product as a combination product consisting of a drug constituent part (the diphoterine solution) and a device constituent part (the aerosol spray canister). Further, consistent with section 503(g)(1) of FD&C Act and FDA's implementing regulations, because the primary mode of action of the combination product is attributable to the drug solution, FDA designated CDER as the lead Center for premarket review and regulation of the product.

As you note, in September 2012, the U.S. District Court for the District of Columbia remanded the Diphoterine Skin Wash classification decision to the Agency for further consideration. Upon reconsideration, the Agency issued a revised classification decision that includes a detailed discussion of the scientific grounds for FDA's determination, and which we believe complies with the court's order.[4] As FDA works to finalize the draft guidance documents referred to in the response to Question a., the Agency will make revisions as necessary in light of the U.S. District Court for the District of Columbia's September 2012 ruling.

f. Despite the court ruling, FDA has persisted in its determination that the portable body shower be classified as a drug. In response to the ruling, FDA created a new "meaningful contribution" standard for determining if a product is a device. Please explain how FDA developed its "meaningful contribution" test and what criteria FDA will apply in determining whether that test is met. How is it that FDA can reinterpret statute seemingly at will?

As noted above, the product to which you refer—Diphoterine Skin Wash—is not a "portable body shower." It is comprised of a pressurized canister that delivers a diphoterine solution onto the skin as an aerosolized mist. It is intended to help prevent or minimize accidental chemical burn injuries. The diphoterine solution is expected to react with harmful chemicals to neutralize them, draw chemicals from the interior to the exterior of the skin, and displace chemicals from the body. The device canister aids in delivery of the diphoterine solution by allowing its ready delivery onto the skin. FDA classified the product as a combination product consisting of a drug constituent part (the diphoterine solution) and a device constituent part (the aerosol spray canister). Further, consistent with section 503(g)(1) of the FD&C Act and FDA's implementing regulations, because the primary mode of action of the combination product is attributable to the drug solution, FDA designated CDER as the lead Center for premarket review and regulation of the product.

FDA did not improperly create a new test, but gave effect to the existing statutory language. As explained in the Agency's decision on remand concerning the Diphoterine Skin Wash classification, the statutory definition of device in section 201(h) of the FD&C Act excludes a product that "achieve[s] its primary intended purposes through chemical action within or on the body of man." The device definition does not expressly state how much chemical action suffices for a product to be excluded. To give effect to the statutory language—and to clarify that a *de minimis* amount of chemical action would not exclude a product from the device definition—FDA interprets the device definition to exclude a product if chemical action "meaningfully contributes" to the product's primary intended purposes. In other

[4] https://ecf.dcd.uscourts.gov/cgi-bin/show_public_doc?2011cv1187-26

words, if chemical action meaningfully contributes to a primary intended purpose, the primary intended purpose is achieved through the chemical action.

FDA's reasoning for determining that the diphoterine solution in the Diphoterine Skin Wash product does not meet the device definition is more fully explained in the classification determination issued on remand and referred to in response to Question e. (above). For further information on this matter, we refer you to the court docket (Case No. 1:13-cv-01177 (RMC)).

g. What impact will such draft guidance and the new "meaningful contribution" test have on regulatory predictability? How can manufacturers be sure guidance will not be further revised without their input?

As explained in response to Question f. (above), in using "meaningfully contributes" in its remand decision, FDA did not improperly create a new test but gave effect to the existing statutory language and clarified that a *de minimis* amount of chemical action would not exclude a product from the device definition. Further, the draft guidance documents referred to in the response to Question a. (above) are intended to enhance transparency for stakeholders concerning the factors that FDA may consider in its product classifications. FDA believes that providing greater transparency through guidance that explains the factors that may be considered in product classifications will help to enhance regulatory predictability.

FDA follows its good guidance practices regulation in 21 CFR 10.115, which requires, with certain exceptions, opportunity for public comment on draft guidance. Like other stakeholders, manufacturers may offer input on guidance development through comments on draft guidance, as they have done on the draft guidance documents referred to in the response to Question a (above). Further, as provided in 21 CFR 10.115(g)(5), stakeholders are welcome to offer comments on any guidance at any time for the Agency's consideration.

h. How do you propose we use reasonable efforts to harmonize its classification of products as drugs and medical devices with other global regulatory agencies?

FDA has initiated efforts to work on product classification and related issues directly with foreign regulatory agencies and also through international bodies in which both foreign regulators and the regulated industry participate. Challenges for these efforts include differences in the legal authorities that these regulatory bodies implement, including how products are classified and regulated. FDA remains committed to pursuing international regulatory coherence consistent with U.S. law and the promotion and protection of the public health.

i. Could requiring companies to comply with US drug regulations, when they are required to comply with medical devices regulations in all other countries for the identical product, place an unreasonable burden on the companies and could prevent introduction of important products to U.S. patients?

Some products that are regulated as drugs in the United States are regulated as devices in other countries and vice versa. FDA classifies products in accordance with the statutory definitions in force in the United States. We seek to implement our regulatory programs for drugs and devices in a manner that is consistent with U.S. law and our mission to protect the

public health, without imposing undue burden. We have developed regulatory programs to facilitate the development and availability of important products for U.S. patients. These include drug and device review programs. We remain committed to pursuing efforts with foreign counterparts to pursue regulatory coherence to minimize regulatory burden consistent with U.S. law and the promotion and protection of the public health.

27. **Has the agency taken any specific action to promote the development of treatments related to Duchenne Muscular Dystrophy? Specifically, has the agency considered using its accelerated approval process authority in FDASIA to promote the development of Duchenne Muscular Dystrophy given the challenges of designing and populating a Phase III clinical trial with these patients? What successes, challenges and setbacks has the agency encountered in this area?**

FDA has been working closely and extensively with Duchenne Muscular Dystrophy (DMD) drug developers, advocacy groups, researchers, and others to assist in the development of products to treat DMD. Some of these efforts have included (but are not limited to):

- Frequent meetings and communications with drug developers
- Intensive discussions with drug developers regarding suitable clinical trial designs and appropriate clinical trial endpoints
- Participation in scientific meetings and educational programs with researchers and advocacy groups
- Meetings with parents of boys with DMD

As with other rare diseases, there are a number of challenges associated with drug development in DMD. The number of patients available for participation in clinical trials is small. The progression of the disease tends to be slow, and the pace of progression varies from patient to patient on the basis of age and other factors, many of which are not understood. It has been difficult to select a reliable method for evaluation of patients that would demonstrate the positive effects of a drug treatment and be applicable to all patients. Although our understanding of the pathophysiology of the disease is improving, it is still incomplete. We are making progress toward understanding the role of biomarkers in assessing the state of the disease, but our knowledge is still evolving. Finally, DMD is a disease that predominantly affects children, a vulnerable population requiring special protections.

Regarding use of the accelerated approval pathway, drugs and biological products (both referred to as "drugs") may be granted accelerated approval upon determination that the drug:

> "...is for a serious or life-threatening disease or condition... upon a determination that the product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments."[5]

[5] 21 U.S.C. 506(c)(1)

We consider DMD to be a serious and life-threatening disorder and recognize that there are currently no approved drugs specifically for its treatment. We are aware that there are substantial unmet medical needs for this disease and of the urgent needs of the patients.

We note that drugs granted accelerated approval must meet the statutory standards for safety and efficacy, which generally requires evidence obtained from adequate and well-controlled clinical trials. It is largely the type of endpoints used to reach that standard that differs between the two approval pathways: accelerated approval typically relies on endpoints for which validity is not fully established or for which there is greater uncertainty about the correlation of the endpoint with the ultimate outcome. In addition, accelerated approval is subject to the requirement that the drug be studied further to verify and describe its clinical benefit. Consequently, the accelerated approval mechanism does not permit circumventing the regulatory requirements: 1) to conduct an adequate and well-controlled trial with a surrogate endpoint or an intermediate clinical endpoint prior to the product's approval, and 2) to conduct a confirmatory clinical trial to verify and describe the drug's clinical benefit after the approval.

A number of products have been in development for DMD, and we continue to actively engage with sponsors of drugs for treatment of DMD and the patient community.

The Honorable Frank Pallone, Jr.

1. **How much has the biosimilars program received in user fees in FY 13 and FY 14 to date?**

   Biosimilar User Fee Act (BsUFA) fees collected in FY 2013 and FY 2014 as of December 24, 2013:

   -FY 2013 (33 initial biosimilar product development (BPD) fees)-$6,464,040
   -FY 2014, as of December 24, 2013 (31 invoices billed for FY 2014 + 8 initial BPD fees) ($1,735,280 + $6,724,210) = $8,459,490

2. **For FY2013, the FDA committed to find the $20 million "trigger" monies from within their FY2013 appropriations if additional monies were not appropriated by Congress for biosimilars. Has that occurred?**

   Yes. In FY 2013, FDA allocated and obligated $28,040,547 in appropriated funds (excluding user fees) for the process, for the review of biosimilar biological product applications.

3. **What is FDA's commitment for 2014, and subsequent years through 2017?**

   Assuming that the commitment in this question refers to the amount of budget authority and not to performance commitments, the FDA spending trigger will be adjusted each fiscal year as specified in statute (see §§744G(1) and 744H(e)(2)(B) of the FD&C Act). This adjustment takes into account inflationary increases in the overall economy, using the Consumer Price Index. Thus, the commitment for FY 2014 will be $20,000,000, multiplied by the adjustment factor applicable to FY 2014.

The Honorable Marsha Blackburn

1. **FDA's draft bioequivalence guidance for cyclosporine ophthalmic emulsions has been questioned by patient and provider groups, such as the American Academy of Ophthalmology, the American Glaucoma Society, the American Society of Cataract and Refractive Surgery, and the American Optometric Association. As health and safety concerns have been raised, does the agency plan to publicly withdraw the draft guidance and reconsider the matter?**

   Under FDA's good guidance practices (21 CFR 10.115), the intent of a draft guidance is to describe FDA's thinking and scientific recommendations on a particular topic and solicit input from the public on those recommendations. Typically, FDA announces the availability of draft guidance in the *Federal Register* and opens a public docket to collect comments on the topic from industry, stakeholders, and the general public; FDA reviews these comments and prepares a final version of the guidance document that incorporates suggested changes, when appropriate. FDA will carefully consider all submitted comments on the draft BE guidance for cyclosporine ophthalmic emulsion.

2. **How much has the agency collected in user fees for the biosimilars user fee program in FY2013 and how much has been collected thus far in this fiscal year?**

   BsUFA fees collected in FY 2013 and FY 2014 as of December 24, 2013:

   -FY 2013 (33 initial biosimilar product development (BPD) fees)-$6,464,040
   -FY2014 as of December 24, 2013 (31 invoices billed for FY 2014 + 8 initial BPD fees) ($1,735,280 + $6,724,210) = $8,459,490.

The Honorable Gene Green

1. **Section 575 of the FDA Safety and Innovation Act allows the FDA to designate new medical gases after "taking into account any investigational new drug application ... for the same medical gas submitted" under certain conditions. This is a very broad power to be exercised by the Secretary of the Department of Health and Human Services. Once designated, the gas and its use would be immediately generic and available for use by all companies, undermining the significant financial and resource investments made by companies or universities in bringing new medical gases to market. These entities typically have the legal protections provided to the medical drug industry for intellectual property related to INDs. But, this power, if exercised, would eliminate those protections. I understand that the FDA declined to address this important issue in its "Guidance for Industry: Certification Process for Designated Medical Gases," stating: "This document does not discuss how FDA plans to implement its new authority to designate gases... "**

   Moreover, in a written response to Members of this Subcommittee inquiring about this issue, the FDA acknowledged that these concerns are real and that the exercise of this authority could "lead to losses for the persons or entities that have invested resources in that IND ... and could disincentiveize others from pursuing IND... applications for new

medical gases in the future." Yet the response also leaves ample room for FDA to exercise its authority and do just that.

Will you assure Congress that the FDA does not intend to undermine pending and legitimate INDs by listing the medical gas in question under its section 575 (H) authority? Upon finding a pending and legitimate IND, will you allow the IND process to proceed normally, enabling an entity to bring the medical gas to market, protect its research and realize its investment?

We interpret the statutory requirement to "tak[e] into account" any IND or investigation new animal drug (INAD) applications before deeming a medical gas a "designated medical gas" to mean that we should carefully consider the possible negative impacts on new drug development prior to taking such action. We will weigh these potential impacts against the public health benefits of designating a new medical gas, and we note that we cannot pre-judge the outcome of this review for any particular medical gas.

<u>The Honorable Michael C. Burgess</u>

1. **It is my understanding that early clinical trials for many rare diseases are only being conducted outside the United States. Many times, the challenge is differences in how the flexibility in international guidelines are applied in the U.S. for first in human studies. How can the FDA improve its flexibility to ensure that U.S. patients have access to these potentially lifesaving clinical trials?**

From October 1, 2012, to October 1, 2013, CDER received approximately 350 initial IND applications for clinical trials in rare diseases.[6] Of these applications, approximately 95 percent moved forward after the required 30-day review period. That is, only a small number of rare disease initial IND applications were subject to clinical hold[7] on first submission to FDA.

FDA does not have access to numbers and types of INDs (or similar regulatory submissions) submitted to international regulatory agencies, and the rules governing initiation of clinical trials vary by country and/or region. FDA does not have access to data on how many IND applications are submitted first to rest-of-the-world versus the United States (and vice versa).

The reasons for submitting an initial clinical trial to one country or another are many and are under the control of the drug sponsor. For example, first-in-human trials for new products for rare diseases are usually very small (e.g., may include fewer than 10 patients) and are commonly

[6] Point of clarification: CDER receives tens of thousands of IND submissions every year, which includes submissions across the spectrum of clinical development from first administration of a product to human subjects through to late IND phase and post-marketing application updates. Approximately 5,000-6,000 of these IND submissions are "initial" INDs, which include first-in-human and first-in-disease applications, as well as repurposing of drugs (both approved, usually for other purposes, and drugs in development for which there may be existing human experience). October 1, 2012, was the date when it was possible to approximate rare versus common disease IND applications in CDER's database.

[7] 21CFR 312.42, Clinical holds and requests for modification. "A clinical hold is an order issued by FDA to the sponsor to delay a proposed clinical investigation or to suspend an ongoing investigation." Clinical hold can be imposed for one or more of the following reasons: 1) human subjects are or would be exposed to an unreasonable and significant risk of illness or injury, 2) the clinical investigators are not qualified to conduct the IND, 3) the investigator brochure is misleading, erroneous, or materially incomplete, 4) the IND does not contain sufficient information required under regulations (312.23 IND content and format) to assess the risks to human subjects, 5) the IND is for the study of an investigational drug intended to treat a life-threatening disease that affects both genders and men or women with reproductive potential are excluded from eligibility.

conducted at only one or two centers initially. In some cases, sites may be selected based on where experienced treatment centers and/or experts reside, or that may have close geographic proximity to the drug sponsor, in addition to other scientific considerations.

As explained in FDA's regulations, for drugs intended to treat life-threatening and severely debilitating illnesses, FDA "has determined that it is appropriate to exercise the broadest flexibility in applying the statutory standards, while preserving appropriate guarantees for safety and effectiveness."[8] FDA has a long and well-documented history of applying flexibility to the development of new products that applies to early IND phases, through to marketing application review. This is evidenced by the fact that most novel products are approved in the United States first prior to rest of the world, and FDA has approved more orphan drugs than any other international regulatory agency. FDA is ready and willing to engage with drug sponsors to discuss initiation of clinical trials for drugs to treat rare diseases under a U.S. IND. FDA has the best developed mechanism for providing drug development advice than any regulatory agency in the world. Each year CDER conducts over 2,000 formal meetings to discuss drug applications; the vast majority of those meetings occurring during the development phase and many occurring before an IND is submitted (so-called pre-IND meetings).

We continue to work closely with drug developers through formal meetings and use of expedited programs, such as fast track and Breakthrough Therapy (BT) designations, to try to find efficient pathways forward for drug development, while not subjecting patients to unreasonable risks.

We additionally note that patient access to investigational agents outside of a clinical trial (Expanded Access or EA) is an additional option for patients with serious diseases who may not qualify for a clinical trial. There are several considerations for EA; however, important among them being that the drug's sponsor must be willing to supply the drug and that EA not interfere with the commercial development of the product.[9] We remain willing to work with drug developers to explore all available avenues for drug development and access, as appropriate, for rare serious disorders.

2. **What is the FDA assessment to date of the impact of Breakthrough therapy designation to expedite the availability of life-saving medicines to patients? Given that many more breakthrough therapy designations have been granted than was anticipated-has this had an impact on the availability of resources for each designation (i.e. are they able to actually spend as much additional time on each as they had intended)? Has the high number of designations led to a prioritization of certain products with the designation over others with the designation?**

As of July 11, 2014, FDA granted 56 designations under the BT program, and six drugs with BT designation have been approved by FDA. Many of the drugs that have received BT designation so far under the new program have been relatively late in their development, including in some cases, drugs for which a marketing application had already been submitted and, therefore, could not fully benefit from this new program's features. With time, FDA expects that most of the new BT designations will be for drugs that are early in their clinical development, which will provide a

[8] 21 CFR 312.80 Drugs intended to treat life-threatening and severely debilitating illnesses.
[9] Guidance for Industry, Expanded Access to investigational drugs for treatment use—Qs & As.
http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM351261.pdf.2013.

better assessment of the impact of the BT designation in helping to speed the development and approval of these promising new drugs.

FDA has been surprised by the number of drugs that have qualified for designation; the number has far exceeded predictions that were made at the time the legislation was developed. Of course, having a larger number of promising new drugs for patients with serious and life-threatening diseases with unmet medical need is a good thing for patients and for public health. FDA is committed to continuing to fully implement the BT program and will work to balance this new program with other Agency priorities.

3. What is the FDA assessment to date of the impact of "The Program" for NMEs and Original BLAs to expedite the availability of life-saving medicines to patients?

The PDUFA V goals letter, agreed to by FDA and the regulated industry, states that the goal of the Program is to "...improve the efficiency and effectiveness of the first cycle review process and decrease the number of review cycles necessary for approval..." The idea behind the Program was that better pre-submission planning, submission of complete applications, improved communication and transparency between the applicant and review team during review, and additional review time will improve the efficiency of the first review cycle, which may decrease the number of additional review cycles prior to approval. The Program began with applications received on or after October 1, 2012. Therefore, to date, only a few applications have completed the review process and received an action from FDA. The early indications are that the Program has been implemented as agreed and that the specific opportunities for communication between FDA and applicants have contributed to review efficiency and are valued by both parties. FDA and industry will have a more complete assessment of the Program when the interim assessment in FY 2015 better characterizes the range of experience in the Program.

4. What is the FDA assessment to date of the impact of the Patient-Centered Drug development goals in the FDA performance goals and other patient-centered components of FDASIA?

By the end of FY 2013, FDA had conducted four meetings on patient-focused drug development (PFDD). The meetings addressed the severity of disease and the unmet medical need for myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS), lung cancer, HIV, and narcolepsy. Based on the overwhelmingly positive feedback that FDA has received from patient advocates who participated in the meetings to date, and their positive reviews of the meeting reports published to date, we believe that this initiative is achieving its aim to increase the opportunity for direct and informative input from patients to FDA drug review considerations. FDA conceptualized PFDD to ensure that the Agency heard from patients outside the context of a specific drug under Agency review. The PFDD meetings are serving that purpose. FDA announces all PFDD meetings in a *Federal Register* notice that includes specific questions on which the Agency seeks feedback from the patient community. FDA obtains this feedback at the meeting and through a public docket for written submissions. In some cases, patient groups have used these questions to create survey instruments of their patient communities. This information helps FDA characterize the context in which regulatory decisions are made for each disease area discussed in a PFDD meeting. This context is an important part of regulatory decision-making and is represented in a PFDD report written by FDA that summarizes what we heard in PFDD meetings and submissions to the docket. The 'Voice of the Patient' reports are available at *http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm368342.htm.*

5. I am concerned about the recent FDA decision to recommend the upscheduling of hydrocodone combination products. Patient access continues to be a concern for patients, as well as physicians if hydrocodone-containing medications are indeed rescheduled.

a. The FDA has made its recommendation to reschedule these medications. However, the agencies' report justifying your recent decision has not been made public. When will this report be sent to HHS? When will this report be made public?

The scientific and medical evaluation and scheduling recommendation (which recommends up-scheduling of hydrocodone combination products, and with which the National Institute on Drug Abuse concurred) was prepared by FDA and sent to HHS on December 11, 2013. HHS transmitted the document to DEA on December 16, 2013. On February 27, 2014, DEA published a notice of proposed rulemaking to reschedule hydrocodone combination products from Schedule III to Schedule II, with a public comment period that ended April 27, 2014. DEA's notice can be found at this website: *http://www.gpo.gov/fdsys/pkg/FR-2014-02-27/pdf/2014-04333.pdf*. Both the DEA and HHS analyses are available in their entirety in the public docket for this proposed rule (Docket No. DEA–389) at *http://www.regulations.gov/#!documentDetail;D=DEA-2014-0005-0001*. On August 22, 2014, DEA published the final rule rescheduling hydrocodone combination products from schedule III to schedule II of the Controlled Substances Act. *http://www.gpo.gov/fdsys/pkg/FR-2014-08-22/pdf/2014-19922.pdf*.

b. I am not aware that the FDA has access to new scientific research showing that rescheduling would address prescription drug abuse and diversion of these drugs. Will you provide us with any new information on any new scientific data FDA has that suggests rescheduling these products will substantially curb misuse and abuse?

As an initial matter, it is important to clarify that FDA prepared the scientific and medical evaluation and scheduling recommendation for hydrocodone combination products under the requirements of the Controlled Substances Act (CSA) and the Food and Drug Administration Safety and Innovation Act (FDASIA), neither of which requires that scheduling recommendations be supported by evidence that rescheduling a drug would address abuse and diversion and substantially curb misuse or abuse. However, FDASIA did require that, in preparing the scientific and medical evaluation and scheduling recommendation required under the CSA,[10] the Secretary of HHS must solicit input from a variety of stakeholders on the health benefits and risks, including the potential for abuse and

[10] The Secretary of HHS is required to consider eight factors in the scientific and medical evaluation:
1. The drug's actual or relative potential for abuse
2. Scientific evidence of the drug's pharmacological effects
3. The state of current scientific knowledge regarding the drug or other substance
4. The drug's history and current patterns of abuse
5. The scope, duration, and significance of abuse
6. What, if any, risk there is to the public health
7. The drug's psychic or physiologic dependence liability
8. Whether the substance is an immediate precursor of a substance already controlled

the impact of the upscheduling of hydrocodone combination products. To satisfy this requirement, FDA held an advisory committee meeting on January 24-25, 2013, which provided opportunity for public comment. The Advisory Committee itself included members with scientific expertise in areas relevant to opioid abuse, including representatives from the National Institute on Drug Abuse, the Centers for Disease Control and Prevention, and a patient representative. The Committee voted 19 to 10 to recommend that hydrocodone combination products be placed into Schedule II. In addition to public commentary at the meeting, 768 comments were submitted to the Docket and to two other related dockets by patients, patient groups, advocacy groups, and professional societies.

FDA recognizes that the rescheduling recommendation, if implemented by DEA, is only one piece of the many activities that are needed to address opioid abuse. We agree with the important need to continue to monitor the impact of the action to minimize the unintended negative impact of patients who need pain relief.

c. Will you provide us with any new scientific data the agency has that addresses the potential impact rescheduling will have on patient access to these medications?

There are differences in the laws and regulations that govern how drugs under schedules II and III may be prescribed and refilled. However, fully predicting the public health impact of this action, including the impact on access by legitimate patients, is complicated by the many factors that shape prescribing patterns for hydrocodone, including reimbursements by payers, guidelines promulgated by societies, patterns of prescription, and laws enacted at various levels of government. An example of this is the challenge that can be seen in trying to predict how the decision to reschedule will be interpreted and responded to by prescribers. At the Advisory Committee held in January to discuss this issue, some commenters voiced the hope that rescheduling would reset the understanding of prescribers about the potential adverse effects of misuse of hydrocodone combination products. Others voiced concerns that rescheduling would drive the increased prescription of more single-entity products containing a higher dose of opioids (e.g., oxycodone, oxymorphone, methadone). Still, others voiced concerns about the impact of rescheduling on the availability of treatments for pain patients.

FDASIA did require that, in preparing the scientific and medical evaluation and scheduling recommendation for hydrocodone combination products, the Secretary of HHS solicit input from a variety of stakeholders on the health benefits and risks, including the potential for abuse and the impact of the upscheduling of hydrocodone combination products. As discussed above, the scientific and medical evaluation and scheduling recommendation, is generally made public as part of DEA's rulemaking process.

d. How can the FDA prevent the rescheduling from having a negative impact on patients in nursing homes who need opioid analgesics?

While DEA is charged with the enforcement of the provisions under Schedule II of the CSA, FDA has discussed the issues regarding appropriate access to pain medicines, including opioids, with groups that represent the health care professionals that care for patients in nursing homes and other extended care facilities and agrees that is it is important to continue to work to assure that appropriate access to pain medicines for appropriate patients is maintained.

6. **In April, you determined that OxyContin was an abuse deterrent formulation. You later made a determination that Opana reformulation did not meet your standard. Then you recently approved Zohydro, an extended release ER single entity hydrocodone with no abuse deterrent products and that industry, both innovator and generic, need to have a clear understanding of FDA's standard. I am concerned that the current regulatory requirements are so confusing that innovators may just walk away from developing abuse deterrent formulations. When you approve non-deterrent products it seems like a step backwards. Will you provide more detail on the standard that is being applied by the FDA in this realm?**

Please see the above responses to Questions 15e and f from the Honorable Joseph R. Pitts, which explain FDA's case-by-case approach to evaluation of opioids with and without abuse-deterrent properties. Under FDA's current approach, abuse potential is one aspect of a product's safety that FDA considers, together with all other appropriate factors, in determining whether a product's benefits outweigh its risks. As the science of abuse deterrent technologies continues to develop, we will continue to evaluate our approach to regulatory decisions concerning these products.

While FDA strongly supports a transition to abuse-deterrent opioids, we do not believe it is feasible or in the interest of public health to require all products in the class to be abuse-deterrent, at this time. In light of the need for further data and scientific development in this nascent and rapidly evolving area, FDA intends to continue to take a product-by-product approach to regulatory decisions concerning the safety and effectiveness of opioid products.

Regarding your concern that our regulatory approach may deter innovation, we can report that we are observing a lot of development activity in the area of ADF development. We believe that our current policy provides sufficient incentives for the development of abuse-deterrent drug products while preserving access to a range of therapeutic agents for patients in pain.

7. **Section 901 of the FDA Modernization Act of 1997 (FDAMA) as amended by the FDA Safety and Innovation Act (FDASIA) creates a clear pathway for treatments for rare diseases to receive accelerated approval. The first criteria is that the disease be rare and life threatening. As you know, Duchenne Muscular Dystrophy affects approximately one in every 3,500 boys and is always fatal. In your view, does Duchenne meet this criteria?**

Please see FDA's response to Question 27 from the Honorable Joseph R. Pitts.

We additionally note that the first requirement for a product to be considered for accelerated approval is that a product be for a serious or life-threatening disease or condition. While there is no requirement that the disease be rare, in recent years the accelerated approval pathway has been used most frequently for rare conditions (see FDA response to Question 2 from the Honorable Gus Bilirakis).

The Honorable Phil Gingrey

1. **On June 12, 2013, in the Federal Register, FDA published a proposed rule titled "Establishing a List of Qualifying Pathogens under the Food and Drug Administration**

Safety and Innovation Act." In section C of the Proposed Rule, the Agency states that"... inclusion of a pathogen on the list of 'qualifying pathogens' does not determine whether a drug proposed to treat an infection caused by that pathogen will be given QIDP designation." In the same section of the Proposed Rule, the Agency further states "... the development of a treatment for an infection caused by the pathogen included in the list of 'qualifying pathogens' is neither a necessary nor a sufficient condition for obtaining QIDP designation ... " In essence, does the Agency consider the list as having any real bearing to qualified infectious disease product (QIDP) designation?

As explained in the Proposed Rule, which was finalized on June 5, 2014, the statutory standard for inclusion on FDA's list of qualifying pathogens is different from the statutory standard for QIDP designation:

- QIDP designation, by definition, requires that the drug in question be an "antibacterial or antifungal drug for human use intended to treat serious or life-threatening infections" (section 505E(g) of the FD&C Act, as amended by FDASIA).
- "Qualifying pathogens" are defined according to a different statutory standard; the term "means a pathogen identified and listed by the Secretary...that has the potential to pose a serious threat to public health" (section 505E(f) of the FD&C Act, as amended by FDASIA).

Therefore, a drug intended to treat a serious or life-threatening bacterial or fungal infection caused by a pathogen that is not included on the list of "qualifying pathogens" may be eligible for designation as a QIDP, while a drug that is intended to treat an infection caused by a pathogen on the list may not necessarily be eligible for QIDP designation if the proposed use is not for a serious or life-threatening infection. While many drugs that are granted a QIDP designation are likely to be active against one or more qualifying pathogens, a qualifying pathogen may cause some infections that are not serious or life-threatening, and for these uses, a drug would not be eligible for a QIDP designation. The list of qualifying pathogens provides examples of the types of pathogens that cause infections for which treatment might be eligible for QIDP designation.

2. **21 USC 355E(g) provides the definition of QIDP: "The term 'qualified infectious disease product' means an antibacterial or antifungal drug for human use intended to treat serious or life- threatening infections, including those caused by-(1) an antibacterial or antifungal resistant pathogen, including novel or emerging infectious pathogens; or (2) qualifying pathogens listed by the Secretary under subsection (f)." Participants in the legislative process greatly debated this definition, predominantly because the term "serious or life-threatening" is not defined in statute, only in guidance, and therefore could be modified in the future. On the other hand, the statute not only defined "qualifying pathogens," it also set up an elaborate and formal process for determining pathogens that can make the "qualifying pathogen" list. Thus, by stating that "serious or life-threatening infections" include those caused by "qualifying pathogens," Title VIII of FDASIA provided some certainty and transparency early in the clinical development process about which products could be eligible for QIDP designation. If the Agency's proposed interpretation of the statute stands, would not the intended certainty or transparency be lost, and the "qualifying pathogen" list would serve no real purpose and carry no weight whatsoever, making it inconsistent with the intent of Congress?**

The statute provides considerable certainty and transparency in the QIDP designation process. By linking QIDP designation to serious and life-threatening infections, Congress has set a clear benchmark that FDA has significant experience in implementing, with respect to other programs. In addition, by not limiting the definition of QIDP to infections caused by qualifying pathogens, Generating Antibiotic Incentives Now could be implemented immediately after enactment, without having to wait to complete the process of rulemaking to establish a list of qualifying pathogens. In fact, the first QIDP designations were granted on September 8, 2012, just two months after the enactment of FDASIA, and 35 designations have been made within 18 months of enactment.

Moving forward, dependence on the qualifying pathogen list for QIDP designation would be neither practical nor timely. Antimicrobial resistance is constantly changing. Due to the time it takes to complete rulemaking, the list of qualifying pathogens will not necessarily reflect new and emerging public health threats. In contrast, drugs intended to treat serious or life-threatening bacterial or fungal infections caused by pathogens associated with emerging public health threats can be designated as QIDPs without waiting for such pathogens to be added to the list of qualifying pathogens.

3. **Since clinical data is usually limited on resistant infections and generic companies are not about to conduct new clinical trials for old drugs, isn't it critical that FDA also use all the tools at its disposal to set and update breakpoints, tools like pharmaco-metric and pharmaco-dynamic data (PK PO), nonclinical data, and state-of-art statistical methods to both update old breakpoints and as well as to set new breakpoints for products before the FDA for approval?**

As clinical data regarding antibacterial drug susceptibility and available clinical outcome information is often limited, particularly in the case of older antibacterial drugs, FDA considers all available and relevant information, including in-vitro microbiology data, data from animal models of infection, and statistical modeling using PK/PD information to inform the establishment of susceptibility test interpretive criteria. For a particular drug, the amount and quality of any of these four types of information may vary.

4. **The 2012 GAO report found that the Agency was way behind in updating breakpoints. Will you provide the Committee with an update? How many marketed antibiotics are there in the U.S. for which the breakpoint for the product label has neither been confirmed nor updated? What is the agency's plan for getting this done as well as what is FDA's process and plans to update breakpoints moving forward?**

FDA continues to work with pharmaceutical companies so that they can update the susceptibility test interpretive criteria (breakpoints) in their drug labels as expeditiously as possible. There are 207 RLDs for antibacterial drugs for human use marketed at this time. Labeling regarding susceptibility test interpretive criteria has been reviewed and updated for approximately 150 of those drugs, as of June 30, 2014. For the remainder, discussion of FDA recommendations with pharmaceutical companies is in progress or scientific review is underway. The current process of relying upon pharmaceutical companies to submit supplements to update the susceptibility test interpretive criteria in their labels is not optimal for a number of reasons:

- Many antibacterial drugs are very old, and they are now marketed only by generic firms. These companies often do not have staff with the technical expertise to evaluate and update the susceptibility test interpretive criteria.

- This approach to updating labeling is very resource-intensive from FDA's perspective. The labeling of each RLD has to be addressed separately when, in fact, the interpretive criteria are often the same for all products containing a specific drug substance, so there is a great deal of duplicate effort.

- In addition to the RLDs, there are approximately 400 additional generic systemic antibacterial drugs. It is expected that each generic firm will update their label when the RLD label for that generic antibacterial drug product is updated. The collective resources that are required of the pharmaceutical companies to update their drug product labeling and the associated FDA resources are/will be considerable, while most of this work will be to simply duplicate work previously performed to update the RLD label.

In 2009, FDA published a guidance for industry, "Updating Labeling for Susceptibility Test Information in Systemic Antibacterial Drug Products and Antimicrobial Susceptibility Testing Devices," that lays out a process for updating susceptibility test interpretive criteria in accordance with the requirements of FDAAA. This process involved the recognition by FDA of susceptibility test interpretive criteria established by standard development organizations. This recognition would be published in a *Federal Register* notice, and sponsors would be required to either update their labeling to be in conformance with these standards or submit data to support alternative criteria.

The process outlined in the guidance would still require the management of changes to susceptibility test interpretive criteria through labeling supplements. However, it has become increasingly clear that the package insert may not be the best place to document the current susceptibility test interpretive criteria. FDA would welcome the opportunity to discuss processes that may be more likely to ensure that most up-to-date and accurate susceptibility test interpretive criteria information is made available to clinical laboratories and health care providers.

5. The 2012 GAO report found that FDA had not taken any regulatory action against companies that failed to respond to the agency's efforts to obtain updated breakpoint information. Has the FDA taken any regulatory action against such companies since the publication of the GAO report and if not, why not? What type of regulatory action can the FDA take in this situation?

FDA has not taken regulatory action against the companies that have not yet updated their susceptibility test interpretive criteria. Generally, taking action against a sponsor who failed to update the susceptibility interpretive criteria in its labeling would be resource- and time-intensive. FDA believes that working with the sponsor to update the labeling would generally be more efficient and obtain a more optimal result.

As explained in our 2009 guidance for industry, "Updating Labeling for Susceptibility Test Information in Systemic Antibacterial Drug Products and Antimicrobial Susceptibility Testing Devices," under existing regulations, a sponsor is responsible for updating its drug product's

labeling whenever new information becomes available that causes the labeling to become false or misleading and, therefore, misbranded.

6. **Antibiotic products have a number of challenges in terms of their development that may lead to clinical data not entirely reflective of when a new QIDP candidate may actually work.**

   In antibiotic development, the least sick individuals tend to be in clinical studies to assure that such patients have NOT been exposed to other antibiotic products before the study product is introduced. This "exclusion criteria" that helps power a pivotal clinical trial may also ironically reduce or even exclude the enrollment of patients with resistant infections.

   In other words, a significant amount of potentially relevant clinical data cannot be collected and, therefore, a newly established clinical breakpoint for QIDP product could be inappropriately high. Do you agree that this potential exists, that is setting a new breakpoint too high? How does FDA propose to deal with this situation, whereby the data in clinical studies may be skewed to the least sick patients and then the need for new QIDP product with breakpoints that are not set so high that the sickest do NOT have access to life saving antibiotics?

A number of options for the inclusion of seriously ill patients with unmet medical need in clinical trials are described in the draft Guidance for Industry, "Antibacterial Therapies for Patients with Unmet Medical Need for the Treatment of Serious Bacterial Infections" (available at *http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM359184.pdf).*

In a more streamlined development program targeting serious bacterial infection in patients with unmet need, clinical trial data regarding antibacterial drug susceptibility to the investigational drug and clinical outcome to inform establishment of susceptibility test interpretive criteria may be limited. FDA will also consider other available information, including in-vitro microbiology data, data from animal models of infection, and statistical modeling using PK/PD information, and weigh this information along with the available clinical data in working with the company to establish susceptibility test interpretive criteria for their drug product.

7. **In order to maximize the effectiveness of the GAIN Act, will you clarify that the establishment of breakpoints for such QIDPs would utilize both clinical and additional forms of evidence, as well as rely upon advanced statistical methods as appropriate, to ensure their breakpoints are set appropriately and, importantly, not set too high especially in light of the unique circumstances confronting QIPD product development already outlined?**

FDA weighs all available and relevant information, including clinical data, in-vitro microbiology data, data from animal models of infection, and statistical modeling using PK/PD information to inform the establishment of susceptibility test interpretive criteria. We note that the quantity and quality of all of these different types of information may vary among drug development programs.

8. What steps is the FDA now taking to assure that breakpoints for new QIDPs rely on these other sources of non-clinical data and what has been industry's response?

The draft Guidance for Industry, "Microbiological Data for Systemic Antibacterial Drug Products – Development, Analysis, and Presentation" (available at *http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM182288.pdf)* recommends that pharmaceutical industry sponsors obtain in-vitro microbiology data and data from animal models of infection, and perform statistical modeling using PK/PD information in the development of proposed breakpoints. This information is submitted and considered in the review of a new drug application for an antibacterial drug.

9. Advisory Committee decisions are not binding on the FDA, but three years ago, the Anti-Infective Drugs Advisory Committee decided that "It would not be the best use of resources for FDA to duplicate the work CLSI when, essentially, the same experts would be utilized ... [and] One suggestion was that the Agency should have a working group to routinely evaluate published and unpublished data for each drug class... If interpretation of the data differs among FDA and CLSI, it should be brought before the [Advisory] Committee."

Would it not be appropriate for FDA to rely on such outside expert findings with regard to breakpoints? And isn't it actual practice now for physicians and other health care providers to rely on CLSI and other expert third party breakpoint findings because this information is more up to date and reflective of scientific knowledge than what's on the FDA label for many antibiotic products?

Prior to this Advisory Committee meeting, FDA published a guidance for industry, "Updating Labeling for Susceptibility Test Information in Systemic Antibacterial Drug Products and Antimicrobial Susceptibility Testing Devices," that describes a process by which FDA would recognize certain susceptibility test interpretive criteria "developed by one or more nationally or internationally recognized standard development organizations." In addition to FDA's recognition of these standards, it would be more efficient and effective for the susceptibility test interpretive criteria to be removed from the package insert; the FDA web site would then serve as the standard reference for FDA-recognized breakpoints.

FDA would welcome the opportunity to discuss processes that may be more likely to ensure that most up-to-date and accurate susceptibility test interpretive criteria information is made available to clinical laboratories and health care providers.

10. The growing resistance of several bacterial strains to all or nearly all antibiotics currently approved is a public health emergency. Recently, the Centers for Disease Control and Prevention (CDC) issued an alarming report on this topic, noting that each year at least 2 million Americans acquire a serious infection resistant to one or more antibiotics designed to treat that infection. CDC warned if we do not take steps now, we could be entering a "post antibiotic era."

The FDA has indicated that it agrees that product innovation is one of the keys to solving this situation. In addition to the GAIN Act, what other specific incentives might work to significantly grow antibiotic innovation?

Antibacterial drugs provide value not only in their ability to treat common infections, but also in their support of other life-saving medical interventions such as surgery, chemotherapy for cancer patients, organ transplantation, and the care of premature infants. As a nation, we need to begin to think in terms of promoting the establishment of a sustainable and robust antibacterial research and development enterprise, while also preserving the effectiveness of the antibacterial drugs we have, so that sufficient therapeutic options will be available when future microbial threats emerge. Given the limited number of antibacterial drugs currently in development and the continued and increasing public health threat posed by life-threatening, drug-resistant pathogens, the Agency agrees that additional approaches to help encourage antibacterial drug development should be considered.

One approach to encouraging antibacterial (as well as antifungal) drug development is contained in the recently introduced H.R. 3742, the Antibiotic Development to Advance Patient Treatment Act (ADAPT Act). This approach would establish a distinct pathway for the development of drugs that are intended for use in patients with unmet medical need (i.e., patients with serious or life-threatening infections and few or no available treatment options) based on a streamlined development program. If such legislation were passed, it would be important that such drugs, which are intended for a limited population of patients, include within their labeling a simple and clear way to identify them (e.g., using a distinct labeling statement and/or logo) so that the health care community could self-limit their use to situations where the drugs' risk/benefit profile is clinically supported. It also would be important that the promotional materials for such products undergo pre-dissemination review.

12. **As part of the 2012 MDUFA Goals letter, FDA agreed to new performance metrics for 510(k) and CLIA Waiver dual submissions. An important part of the commitment letter that FDA signed with industry is the issuance of a Guidance by FDA that will help industry understand the requirements of successfully completing dual 510 (k) and CLIA waiver applications.**

    These two provisions will aid the public health through quicker review times and potentially more tests available to doctors and patients. A number of rapid tests for diseases listed in the CDC's recent report on antibiotic resistant pathogens are either in the review process or are nearing the point of submission.

    We understand FDA believes this Guidance will be delayed because of issues related to the information technology required for its application tracking system. What are those issues and why would this delay the issuance of a Guidance designed to facilitate the overall management of these applications? As part of dual submissions with a 510(k) application, can CLIA waivers be tracked manually if 510(k)s are tracked electronically? What are FDA's plans to meet the obligations of this FDA/industry agreement if Guidance is not issued?

The 2012 MDUFA Goals letter (the "MDUFA III commitment letter")[11] did not specify a timeline associated with publishing the CLIA-related guidance.

However, the Center for Devices and Radiological Health (CDRH) has prepared an update to the Guidance for Industry and FDA Staff: "Administrative Procedures for CLIA Categorization."[12] This updated guidance includes changes to the administrative procedures for CLIA categorizations as well as administrative procedures for CLIA Waiver by Applications and Dual 510(k)/CLIA Waiver by Applications. The Agency published this guidance in March 2014 to coincide with the launch of CDRH's new IT system for tracking all CLIA work, so that performance can be reported as accurately as possible. The guidance includes administrative procedures that are specific to the new IT system.

Of note, the MDUFA III commitment letter refers to a pre-submission prior to submission of a Dual 510(k)/CLIA Waiver by Application. FDA has been reviewing the Pre-submissions that the Agency has received to date and will continue to provide feedback to, and participate in discussions with, sponsors, with regard to any potential Dual 510(k)/CLIA Waiver by Application plans through the Pre-submission program. Such feedback/discussion is actually tailored to the sponsor's specific device, and therefore, is more substantive than the type of information presented in guidance documents. In addition, FDA has been applying the CLIA Waiver by Application performance goals, as outlined in Section II(E) of the MDUFA III commitment letter, since October 1, 2013, the start of MDUFA III.

The Honorable Leonard Lance

1. **To be in compliance with FDASIA, the FDA must allow for novel approaches to use pathophysiologic and pharmacologic evidence to support the use of a biomarker endpoint when the low prevalence of disease makes the existence of other types of data impractical to collect. What kinds of novel approaches is the FDA planning to take to allow for the use of surrogate endpoints in clinical trials for rare diseases?**

FDA is open to and promotes the use of surrogate endpoints and biomarkers in clinical development programs for both common and rare diseases. As explained in our regulations, for drugs intended to treat life-threatening and severely debilitating illnesses, FDA "has determined that it is appropriate to exercise the broadest flexibility in applying the statutory standards, while preserving appropriate guarantees for safety and effectiveness."[13] FDA has a long and well-documented history of applying flexibility to the development of new products for rare diseases, which includes the use of biomarkers and surrogate endpoints in clinical trials, as well as other tools such as non-traditional trial designs. We continue to work with drug sponsors to find ways to apply this flexibility, where appropriate.

Rare disease drug approvals also have a long history of use of biomarkers as surrogate endpoints to support approvals, including traditional and accelerated approvals, and in recent years, many rare

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[11] FDA, "MDUFA Performance Goals and Procedures" (April 18, 2012), available at *http://www.fda.gov/downloads/MedicalDevices/NewsEvents/WorkshopsConferences/UCM295454.pdf.*

[12] FDA, "Guidance for Industry and FDA Staff; Administrative Procedures for CLIA Categorization" (March 12, 2014), available at *http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm070889.pdf*

[13] 21CFR 312.80, Drugs intended to treat life-threatening and severely debilitating illnesses.

disease clinical development programs have relied upon surrogate biomarkers (please see response to the Honorable Gus Bilirakis, Questions 2 and 3 and Appendix 1, for a listing of recent rare disease approvals).

We note that a challenge associated with the use of surrogate endpoints in rare diseases is that there needs to be some empirical evidence to support the biological plausibility of the relationship between the disease, the endpoint, and the desired effect, and clinical data should be provided to support a conclusion that a relationship of an effect on the surrogate endpoint to an effect on the clinical outcome is reasonably likely.[14] In the rare disease field, there is often a lack of sufficient translational science development and understanding of the diseases' pathophysiology, natural history, and other data to support proposed surrogate endpoints. FDA has a number of initiatives in place to promote development of biomarkers, improve data collection in the natural disease studies and registries, and for the development of other translational science, such as the Critical Path Initiative (and other initiatives listed in the response to the Honorable Leonard Lance, Question 2).

2. How will the FDA ensure the upcoming FDA Rare Disease meeting in January will improve the regulatory process for rare disease, when the FDA held a similar meeting in 2010 and issued a report with recommendations, but has yet to implement any of the recommendations more than three years later?

The Public Workshop on Complex Issues in Rare Disease Drug Development was a 3-day meeting that was held January 6-8, 2014.[15] [16] This meeting was held in response to 1) PDUFA V performance goals (Section IX.E.4[17]), and 2) FDASIA Sec 510.[18] Both PDUFA V and FDASIA multi-stakeholder (e.g., industry, FDA, Congress, advocacy) negotiations emphasized that the meetings should be collaborative, include discussions of difficult and complicated issues in rare and pediatric rare disease drug and biologic product and medical device development, and should involve diverse panels of experts from industry, academia, advocacy, and government. The main goals of the public meeting were to foster discussion, hear diverse perspectives from experts, and for pediatric rare diseases (per statute), use the interactions to develop a strategic plan to encourage and accelerate development of pediatric rare disease therapies. Consistent with the FDASIA/PDUFA V negotiations, FDA convened the Public Workshop and included diverse panels of experts from across the broad rare disease stakeholder community (see Appendix 1, Public Workshop on Complex Issues in Rare Disease Drug Development roster).

Also consistent with the FDASIA/PDUFA V negotiations, the overall structure of the meeting and major topics addressed included the following:

1) Day 1: Complex Issues in Rare Disease Drug Development[19]

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[14] Guidance for Industry. Expedited Programs for Serious Conditions –Drugs and Biologics. Draft Guidance.
[15] FDA, Drugs. Public Workshop -- Complex Issues in Developing Drug and Biological Products for Rare Diseases. *http://www.fda.gov/Drugs/NewsEvents/ucm367820.htm*
[16] FDA, Medical Devices. Public Workshop – Complex Issues in Developing Medical Devices for Pediatric Patients Affected by Rare Diseases. *http://www.fda.gov/MedicalDevices/NewsEvents/WorkshopsConferences/ucm367656.htm*
[17] IX. Enhancing Regulatory Science and Expediting Drug Development, E. Advancing Development of Drugs for Rare Diseases
[18] Title V – Pediatric Drugs and Devices, Section 510 Pediatric Rare Diseases
[19] For the final workshop agenda for Days 1 and 2, please see the Public Workshop meeting page, available at *http://www.fda.gov/Drugs/NewsEvents/ucm367820.htm*

a. Session 1: Complex Issues for Trial Design: Endpoints
b. Session 2: Complex Issues for Trial Design: Study Design, Conduct, and Analysis
c. Session 3: Foundational Science
d. Session 4: Safety & Dosing

2) Day 2: Encouraging and Accelerating Development of New Therapies for Pediatric Rare Diseases

a. Session 5: Networks and Collaborations in Support of Pediatric Clinical Trials
b. Session 6: Tolerating Risk and Uncertainty in Pediatric Clinical Trials
c. Session 7: Pediatric Oncology
d. Session 8: Gene Therapy Trials in Pediatric Patients

3) Day 3: Complex Issues in Development of Medical Devices for Pediatric Patients Affected by Rare Diseases[20]

a. Session 1: What's Happening Clinically
b. Session 2: HUD/HDE Discussion
c. Session 3: Engineering Considerations
d. Session 4: Clinical Trials Issues Panel
e. Session 5: Needs Assessment
f. Session 6: Diagnostic Devices
g. Session 7: What Can be Done? Incentives and Otherwise

Issues encountered in rare disease drug development are multi-factorial and complex, and occur across the entire spectrum of rare disease research, beginning in early phase of basic scientific research, through translational scientific research and development, and then later on, into pre-clinical and clinical drug development. Since rare diseases have a long-standing history of under-representation in research and development (R&D), many of the approximately 7,000 rare diseases have no or very limited R&D ongoing, and most have no drug development in progress.

FDA's involvement generally begins when testing of investigational agents in human subjects begins, which typically occurs after many years of basic and translational scientific research have taken place. FDA recognizes and takes extremely seriously its role and responsibilities in the larger drug development process. We also recognize that scientific research and drug development can be greatly facilitated through collaborations of industry, investigators, patients, advocacy groups, and government. While this is true for all scientific research and drug development, the need to collaborate is especially critical for rare diseases where there are small numbers of patients with the individual disorders, opportunities for study and replication are known to be limited, there are few treating physicians and disease experts, and resources are grossly insufficient for the magnitude of the problem.[21] Thus, collaboration beginning early on and continuing throughout drug development, non-proprietary information sharing, and investment into and development of common tools (e.g., endpoint development, biobanking, natural history studies and registries) are especially important given the known limitations in opportunities for research and replication. Meetings, such as this Public Workshop, therefore, play an extremely important role in fostering

[20] For the final workshop agenda for Day 3, please see the Public Workshop meeting page, available at http://www.fda.gov/MedicalDevices/NewsEvents/WorkshopsConferences/ucm367656.htm

[21] There are an estimated 25-30 million Americans living with a rare disease, or approximately 1 in 10 people–this is a substantial public health concern. By comparison HIV affects fewer than 2 million Americans and cancer ~15 million Americans.

collaboration and cooperation, identifying knowledge gaps as well as best practices, and exploring areas where working towards common goals can be best applied. All of these important considerations contribute to the overall rare disease R&D environment.

Regarding the 2010 Open Public Hearing (OPH) on Rare Diseases:

An OPH on rare diseases was held June 29-30, 2010, the purpose of which was for the FDA rare disease internal review group to hear directly from the rare disease community on issues important to them regarding rare disease drug development. The internal review group was convened as part of a legislative requirement.[22] Comments from the OPH as well as all comments submitted to the docket were carefully considered by the review group, and incorporated into review group deliberations, which were later summarized in a report to Congress.[23] A summary of recommendations in three areas from the report is briefly summarized as follows:

1) Increase the foundation of biomedical and regulatory science required to support development and regulatory assessment of medical products for rare disease. This includes:

    a. Development of natural history studies and databases
    b. Identify, develop, and qualify novel biomarkers

2) Increase collaboration among rare disease stakeholders both within and outside FDA.

3) Gain a thorough understanding of the regulatory history of orphan drug products to help identify effective development approaches.

We have made substantial progress in all of the above-listed areas. Some of the progress includes (but is not limited to):

1) Development of Draft Guidance for Industry on common issues in rare disease drug development

2) Conducting a Natural History Studies Workshop in collaboration with NIH in 2012

3) Development of Draft Guidance for Industry on development of natural history studies

4) Creation of a collaborative taskforce for the development of natural history studies between CDER, the National Organization for Rare Disorders (NORD) and NIH's National Center for Advancing Translational Sciences (NCATS) Therapeutics for Rare and Neglected Diseases (TRND) program was formed in 2012 (ongoing).

5) Continuation of work on CDER's Critical Path Initiative (CPI). A draft guidance on the "Qualification Process for Drug Development Tools (DDT)" was published in October 2010,

[22] Agriculture, Rural Development, Food and Drug Administration, and Related Agencies Appropriations Act, 2010, Public law 111-80, Section 740. This Act required FDA to establish an internal review group which "shall recommend to the Commissioner appropriate preclinical, trial design, and regulatory paradigms and optimal solutions for the prevention, diagnosis, and treatment of rare diseases".

[23] A report from the review group is available on FDA's website under the Critical Path Initiative. *http://www.fda.gov/downloads/ScienceResearch/SpecialTopics/CriticalPathInitiative/UCM265525.pdf*

and this provides a description of a formal mechanism for CDER to advise external parties, of any type, how to efficiently develop DDTs that will be useful in drug development. Work on biomarkers, endpoints, and pharmacogenomics through CPI continues on an ongoing basis in numerous areas, such as through participation at conferences and meetings, scientific publications, guidance development and advice, and during individual product development meetings. In particular, CDER's Study Endpoints and Labeling Development program (SEALD) for clinical outcome assessments (COAs) and CDER's Office of Translational Sciences (OTS) for biomarkers are now available to work with outside groups to advance creation of these tools for development of rare disease therapies. Based upon experience with these efforts since then, a revised final DDT qualification guidance was published in January 2014.

6) Initiation of a program by CDER OTS, the Critical Path Innovation Meeting (CPIM), to foster early engagement with drug developers, researchers, advocacy groups, and other components of government who are developing innovative tools (e.g., biomarkers in the exploratory phase of their development and for evaluation under the Biomarker Qualification Program, natural history study designs and implementation, emerging technologies, or new uses of existing technologies, and innovative conceptual approaches to clinical trial design and analysis)

7) Development of an internal FDA staff rare-disease training course, which has occurred annually in CY 2011, 2012 and 2013, and 2014, with the next planned course to occur in March-April 2015. Thus far, hundreds of FDA staff have participated in this training.

8) Formation of an agency-wide Rare Disease Council with representation from CDER, CBER, CDRH, CFSAN and OC. This council, which meets monthly, was formed to foster collaboration between Centers, identify issues of cross-Center interest and develop strategies to address areas of common interest for rare diseases.

9) Co-development of an annual rare disease conference with NORD and the Drug Information Agency that has occurred since 2010. Approximately 300-400 members of the rare disease community (industry, advocacy, researchers, and government) have participated each year. FDA staff also participate in numerous scientific conferences on a variety of rare disease topics.

10) Formation of a CDER-NIH Clinical Center taskforce in 2012, to facilitate research-investigator initiated clinical trials. In addition to scheduled meetings and the development of "early engagement" meetings between CDER and NIH-CC (on a case-by-case basis), this taskforce has resulted in the following:

    a. An IND Regulatory Training program for research-investigators was held in 2013. Presentations from the training program will be made widely available through NIH's website in the future.

    b. FDA posted on its website an IND regulatory training toolkit for investigators.[24]

    c. Emergency IND regulatory tools have also been posted on FDA's website.[25]

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[24] FDA. Drugs. Investigator-Initiated Investigational New Drug (IND) Applications. *http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/InvestigationalNewDrugINDApplication/ucm343349.htm*. 2013.

11) Construction of a CDER database of marketing applications has been completed, which includes extensive application-specific data for new molecular entity and original biologic product marketing applications submitted to CDER from 2007-present. This database allows detailed analyses of critical drug application characteristics (e.g., disease, endpoints, types of trials, regulatory precedents) to inform the development of guidance, advice, processes, and procedures for rare disease drug development. For example, a scientific manuscript on characteristics of rare disease drug applications at CDER was published in 2012.[26]

Since rare disease R&D requires the work and collaboration of so many people from diverse communities, it can be difficult to pinpoint definitive outcomes from one meeting alone. However, we feel that workshops such as the recent Public Workshop of 2014 will play an extremely important role in facilitating, encouraging, and accelerating continued R&D, and building communities and collaborations among rare disease stakeholders. A summary report and a pediatric rare diseases strategic plan will be issued approximately six months after completion of the Public Workshop. FDA remains fully committed to continuing to participate, as resources allow, in the many other collaborative workshops, meetings, and conferences with drug developers, researchers, advocacy groups, and other government agencies on a wide range of biomedical and regulatory science topics that occur throughout the years.

9. As you know, FDASIA included bipartisan language that I advanced with the help of your staff at FDA to resolve a 100-year old issue and create a pathway for medical gases to become approved drugs. I am proud that New Jersey is the home of numerous health care companies that manufacture medical gases used by millions of patients around the country. I am very eager to see the full implementation of these medical gas provisions.

For instance, FDASIA requires that FDA update its current regulations to take into account the unique characteristics of medical gases. FDA is required to report to Congress on the proposed changes in January 2014 and complete all changes by July 2016. FDA's current regulations have caused enforcement issues for decades both for FDA as the regulator and for the regulated community, including expiration dating and calculation of yield. These are issues that must be resolved through amendments to current regulation, as opposed to guidance, in order to provide certainty. I understand that safety organizations representing our New Jersey manufacturers have submitted extensive comments on the changes that are necessary to the current regulations. Will you provide me with an update on progress working with stakeholders to update the necessary federal regulations as well as assure this committee that FDA regulations will be updated to incorporate medical gases by the July 2016 deadline?

Your question refers to FDASIA Section 1112, which requires the Secretary of HHS to: 1) determine whether any changes to Federal drug regulations are necessary for medical gases, 2) submit a report to the Committee on Energy and Commerce and the Committee on Health, Education, Labor, and Pensions regarding any such changes, and 3) to make such changes within four years of the passage of FDASIA (July 9, 2016) "if the Secretary determines…that [such] changes…are necessary."

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[25] FDA, Drugs. IND Applications for Clinical Treatment of a Single Patient in Emergency Setting. *http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/InvestigationalNewDrugINDApplication/ucm343022.htm*, 2013.

[26] Pariser AR, Slack DJ, Bauer LJ, et al. Characteristics of rare disease marketing applications associated with FDA product approvals 2006-2010. Drug Discov Today. 2012;17:898-904.

FDA is conducting an extensive review to determine if changes to the regulations are necessary. After considering numerous suggestions for regulation changes from the medical gas industry, we held a public meeting on this topic on December 6, 2013. We are currently working on the required report to Congress and will determine whether any changes to FDA regulations are necessary for medical gases.

10. I am pleased to hear that certification of medical gas manufacturers is already underway, however I am concerned there is not yet final guidance in place resolving key issues like documentation for subsequent manufacturers. When can Congress expect to see final guidance on the medical gas certification process?

We can assure you that work on this document is ongoing, but we do not have a specific date for issuance of a final guidance. We can report that we addressed the specific issue you mention—documentation expectations for downstream medical gas suppliers (typically transfillers)—with industry representatives at the December 6, 2013, meeting. Our staff is also generally available to discuss this or other specific issues with members of industry as they arise in the course of their regulatory compliance efforts or our regulatory enforcement practices.

The Honorable Bill Cassidy

1. In the event a foreign and domestic manufacturer are similarly situated, such as in the case when both the foreign and domestic manufacturer would be providing an unapproved drug to mitigate a drug shortage, what criteria does FDA consider and use to determine which manufacturer will be permitted by the Agency to provide an unapproved product to mitigate the shortage?

When there is a shortage of a medically necessary drug product,[27] FDA's practice has been to first communicate directly with the current manufacturers of the drug for the U.S. market, which may include both domestic and foreign manufacturers, to work on addressing the shortage. For example, the Agency has asked U.S.-approved manufacturers if they can increase or restart production; if a manufacturer's production has been impacted by quality problems, we have worked with the manufacturer to address those problems and where possible, develop a plan for the product to be released. In rare circumstances, when the current manufacturers that make the drug for the U.S. market have not been willing and able to meet patient needs and an ongoing shortage is anticipated, FDA has explored whether there are other manufacturers, domestic or foreign, already supplying the drug to other countries, who may be able to meet patient needs in the United States. FDA has worked with these manufacturers to determine if they have supplies available for the United States and are able to provide information to FDA to ensure that the drug is of adequate quality, is manufactured in a facility that meets FDA quality standards, and does not pose undue risks for U.S. patients. FDA has then used regulatory discretion to facilitate importation (if necessary) and distribution of the product, on a temporary basis, to meet critical patient needs

[27] A medically necessary drug product is a product that is used to treat or prevent a serious disease or medical condition, for which there is no alternative drug in adequate supply, that is judged by medical staff to be an appropriate substitute. Drug products that are in active shortage are listed on the FDA Drug Shortage Website.
http://www.fda.gov/Drugs/DrugSafety/DrugShortages/ucm050792.htm

during the shortage. The Agency has considered this option only in very limited circumstances. FDA has been reviewing certain aspects of our past practices with respect to importation, in light of the recent decision by the U.S. Court of Appeals for the District of Columbia in Cook v. FDA (733 F.3d 1 (DC Cir. 2013)).

4. **FDA plans to provide expedited entry for Secure Supply Chain Pilot participants, but does not clarify how much faster. Will FDA collect data on how the program impacts clearance rates?**

The Secure Supply Chain Pilot Program (SSCPP) includes an audit process for FDA to determine whether the program has an impact on expediting the importation of certain active pharmaceutical ingredients and finished drug products that are accepted into the program. During the audit process FDA will collect data on the rate of entry release for drugs participating in the pilot, compared with drugs subject to routine drug imports entry review.

5. **The Secure Supply Chain Pilot needs to cover a substantial portion of imports in order to enable FDA to focus its resources on high risk imports. Unfortunately, we are hearing from many qualified companies that the program is not compelling. For companies that plan to participate, the program will cover only a sliver of their imports. In terms of participation rates and amount of trade covered, what are FDA's metrics for success for this program? If FDA does not meet those metrics, is it prepared to pivot to a new, meaningful program, or will it allow the pilot to continue with only a few participants?**

This pilot program applies only to FDA-approved NDAs and ANDAs. The SSCPP is intended to assist FDA in its efforts to help prevent the importation of adulterated, misbranded, or unapproved drugs by allowing the Agency to focus its resources on imported drugs that fall outside the program and may pose risks. If, through our audit process, we find that these firms are capable of consistent compliance with the requirements of this pilot, we may expand the scope of the program to other drug areas. Our initial metrics for success focus on the ability of these firms to comply with the requirements of this pilot program and the FD&C Act, and not necessarily the rate of participation and the amount of trade covered. FDA understands the rate of participation in this program will be small due to its limited application to approved NDAs and ANDAs, but because this is a pilot program, it is adaptable and amenable to change based on the results of our program audit conducted throughout its two-year life cycle.

<u>The Honorable H. Morgan Griffith</u>

1. **While the Senate has now passed and the President has signed into law the Drug Quality and Security Act (H.R. 3204), I am still focused on the overwhelming need to protect patient safety and ensure the drugs patients are receiving are sterile and safe. Many patients rely on the availability of compounded medications to treat a variety of conditions. Without these medications, many patients may not be able to receive treatments they need. Recognizing that both contamination and lack of access may pose serious health risks to patients, how does FDA intend to balance these risks and both**

ensure safe compounded products while maintaining access to products for providers and patients, specifically including access to compounded products for office use?

FDA shares your interest in ensuring that patients receive the drugs they need and that those drugs that are required to be sterile are sterile and are safe. It is important to remember, however, that drugs made by compounders, including those made at human drug compounding outsourcing facilities, are not FDA-approved. When a drug is FDA-approved, patients are assured that FDA has reviewed the safety and efficacy of the drug product and the adequacy of the manufacturing process to produce a quality product prior to marketing. Compounded drugs do not provide such assurance. Therefore, when an FDA-approved drug is available, FDA recommends that practitioners prescribe the FDA-approved drug rather than a compounded drug, unless the prescribing practitioner has determined that a compounded product is necessary for the particular patient and would provide a significant difference for the patient as compared to the FDA-approved drug product.

Under the DQSA, hospitals and health care professionals can purchase compounded drugs without a prescription from a compounder that is registered as an outsourcing facility under section 503B of the FD&C Act. Section 503A requires, among other things, that to qualify for the exemptions under section 503A, there be a prescription for an identified individual patient. The Agency intends to exercise its authority, as appropriate to protect the public health, against compounded drugs that do not qualify for the exemptions in section 503A or section 503B, and drugs that are adulterated or misbranded or otherwise violate Federal laws.

2. **While the DQSA provides clarity on oversight authority for compounding pharmacies, it lacks some much needed clarity on the issue of office use. However, while office use is not mentioned in 503(a), it is expressly permitted under numerous state laws and regulations governing the practice of pharmacy. Will the FDA defer to a state regulatory agency when such a conflict between federal and state law exists?**

FDA is examining its compounding enforcement policies and practices in light of recent outbreaks and the new legislation. We anticipate communicating further with the public as that examination progresses.

3. **H.R. 3204 creates a new class of federally-regulated compounding facilities. These "outsourcing facilities," which will meet the highest possible drug safety standards, will be able to compound a variety of products for physician and patient use. How does the FDA plan to address who is responsible for regulation those entities which are acting like an outsourcing facility but have not voluntarily registered with the agency?**

If a compounder chooses not to register as an outsourcing facility and qualify for the exemptions under section 503B, the compounder could qualify for exemptions from the FDA approval requirements, the requirement to label products with adequate directions for use, and CGMP requirements by meeting the conditions in section 503A of the FD&C Act. Otherwise, it would be subject to all of the requirements in the FD&C Act applicable to conventional drug manufacturers. FDA anticipates that state boards of pharmacy will continue their oversight and regulation of the practice of pharmacy, including pharmacy compounding. The Agency also intends to continue to cooperate with state authorities to address compounding activities that may violate the FD&C Act.

4. **Does the agency intend to petition Congress to expand the definition of an outsourcing facility to include those entities and individuals engaged in the compounding and distribution of non-sterile medications?**

FDA is working to implement the new legislation and has no plans at this time to seek additional legislation.

5. **Does the agency intend to petition Congress to change current language of 503 (b) providing for voluntary registration of an outsourcing facility to a mandated registration?**

FDA is working to implement the new legislation and has no plans at this time to seek additional legislation.

6. **Are outsourcing facilities going to be required to follow Current Good Manufacturing Practices (cGMPs) or, as you indicated in your testimony before the Senate HELP Committee, does the agency intend to promulgate or use a different set of standards with which those firms will be expected to comply?**

Compounders that are registered as outsourcing facilities under section 503B of the FD&C Act are not exempt from section 501(a)(2)(B) of the FD&C Act, which requires compliance with current good manufacturing practice (CGMP). On July 1, 2014, FDA issued a draft interim guidance that describes FDA's expectations regarding compliance with CGMP requirements for facilities that compound human drugs and register with FDA as outsourcing facilities under section 503B of the FD&C Act. The guidance focuses on CGMP requirements related to sterility assurance of sterile drug products and the general safety of compounded drug products.

7. **Repackaging of drug products by outsourcing facilities was not an activity specifically covered in the Drug Quality and Security Act. Given the stringent safety, sterility, and inspection requirements on these facilities, as well as the strong need for access to repackaged sterile drug products by many physicians and patients, will the FDA allow outsourcing facilities to provide sterile repackaged drug products to physicians for administration to patients in treatment settings?**

The Agency is actively reviewing this issue and, in doing so, is taking into consideration the best interests of patients.

The Honorable Gus Bilirakis

5. **Will you tell the Committee what additional advice or guidance FDA plans on doing in the coming year in order for the industry to better understand the FDA's expectations, and encourage submission of applications for bio-similar products? Additionally, is the Agency currently developing, or does it intend to develop, any guidance with respect to unique non-proprietary names?**

FDA is carefully reviewing and considering the comments submitted to FDA's biosimilar guidance and public hearing dockets. We will take into consideration all received comments as we move forward in finalizing the draft guidance documents FDA published in 2012, and in developing future policies regarding biosimilar products and interchangeable products, including guidance on clinical pharmacology data to support a demonstration of biosimilarity to a reference product. FDA is currently considering the appropriate naming convention for biosimilar and interchangeable products licensed under the pathway established by the Biologics Price Competition and Innovation Act of 2009 (BPCI Act).

The Honorable Renee Ellmers

1. **North Carolina is home to thousands of high paying pharmaceutical jobs. We should help find smart ways to make these facilities more competitive. Unfortunately, FDA frequently but unpredictably detains complaint research compounds and active ingredients from highly compliant imports. Section 713 of FDASIA encouraged FDA to address this problem by distinguishing between highly complaint importers and high risk importers, hence the Secure Supply Chain pilot. The application window will close December 31. How have potential applicants reacted to the program? How many have applied? How many do you expect?**

Thus far, industry stakeholders have provided positive feedback and shown great interest in the SSCPP. We received approximately 40 SSCPP applications by the December 31, 2013, deadline.

Additional question asked at the hearing:

During the hearing, Members asked you to provide additional information for the record and you indicated that you would provide that information. For your convenience, descriptions of the requested information based on the relevant excerpts from the hearing transcript regarding these requests are provided below.

The Honorable Joseph R. Pitts

1. **Please submit the Agency's internal spreadsheet tracking all obligations you have under this FDASIA.**

Enclosed

FOOD AND DRUG SAFETY AND INNOVATION ACT (FDASIA) INTERNAL TRACKING SHEET

* User Fee Commitment Letter deliverables are identified via the following Section numbers: PDUFA - 100, MDUFA - 200, GDUFA - 300, BSUFA - 400. User Fee deliverables do not have "statutory" dates and the dates represent agreements in the Commitment Letters.

Item #	Title	Section *	Sub-Section	UFA Goals Letter	Goals Letter Citation	Deliverable Description	Deliverable Type	Statutory Deadline *	Targeted Completion Date **	FDA Completion Due Date **	Responsible Organization	Status ***	Date Completed	Publicly Tracked? (FDASIA TRACK)	FDASIA TRACK Notes (Will be posted on public FDA-TRACK Website)	Public Website Contact
1	I	100		PDUFA	X.A	FDA will begin execution of this plan to implement the benefit-risk framework across review divisions in the pre and post-market human drug review process by the end of the fourth quarter of FY 20 , and the Agency will update the plan as needed and post all updates on the FDA website.	Plan	9/30/2013	9/30/2013	9/30/2013	CDER	Completed	9/30/2013	Y	Completed 09/30/2013 Implementation of this plan is in process http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm325952.htm	http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm272170.htm
2	I	100		PDUFA	IX.B.2	By the end of FY 2013, FDA will hold a public meeting engaging stakeholders in discussing current and emerging scientific approaches and methods for the conduct of meta-analyses, and to facilitate stakeholder feedback and input regarding the use of meta-analyses in the FDA's regulatory review process.	Public Meeting	9/30/2013	11/25/2013	11-25-2013	CDER	Completed	11/25/2013	Y	On November 25, 2013, FDA conducted a public meeting on Meta-Analyses of Randomized Controlled Clinical Trials for the Evaluation of Risk to Support Regulatory Decisions The input from the meeting will be used to develop a draft guidance that describes best practices for the conduct of meta-analyses and FDA's intended approach for the use of meta-analyses in regulatory decision-making. FDA is also publishing a white paper to facilitate discussion at the public meeting, which is available online at http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm390260.htm	http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm272170.htm
3	I	IX		PDUFA	IX.E.2	By mid-FY 2014, FDA, through the Rare Disease Program, will conduct a public meeting to discuss complex issues in clinical trials for studying drugs for rare diseases, including such questions as endpoint selection, use of surrogate endpoints/Accelerated approval, and clinical significance of primary endpoints, reasonable safety exposures, assessment of dose selection, and development of patient-reported outcome instruments.	Public Meeting	4/30/2014	1.8.2014	1/8/2014	CDER	Completed	~	Y	The Public Workshop on Complex Issues in Rare Disease Drug Development was a 2-day meeting that was held January 6-8, 2014. The main goals were that FDA would foster discussion, hear diverse perspectives from experts, and for pediatric rare diseases (per statute), use the interactions to develop a strategic plan to encourage and accelerate development of pediatric rare disease therapies	http://www.fda.gov/DrugsNewsEvents/ucm397620.htm
4	I	100		PDUFA	XI.A.2	By the end of FY 2013, FDA will hold one or more public meetings to include the pharmaceutical industry, other government healthcare providers, patient groups and payers from other sectors of the healthcare delivery system to explore strategies to standardize REMS, where appropriate, with the goal of reducing the burden of implementing REMS on practitioners, patients, and others in various healthcare settings.	Public Meeting	9/30/2013	7/26/2013	7/26/2013	CDER	Completed	7/26/2013	Y	Completed 7/26/2013 To obtain input from stakeholders about REMS standardization and evaluation, FDA held a public meeting to give stakeholders, including health care providers, prescribers, patients, pharmacists, wholesalers, drug manufacturers, vendors, researchers, standards development organizations, and the public an opportunity to provide input on ways to standardize and assess REMS. A link to the information can be found by following this link http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm353*03.htm	http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm353620.htm

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5	I	102		PDUFA	X C	FDA will initiate a public process to nominate a set of disease areas that could benefit from a more systematic and expansive approach to obtaining the patient perspective on disease severity or unmet medical need. FDA will convene 4 meetings per year (CDER will host 17 meetings and CBER will host 3 meetings throughout PDUFA V)	Public Meeting	–	9/24/2013	9/24/2013	CDER	Completed	9/24/2013	Y	This is an annual requirement. FY 2013 was completed 09/24/2013. An FR notice announcing the diseases for FY 14-15 published 4/11/2013 (http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm326192.htm). For FY 2013, the public process was begun with a FR Notice in September 2012 and public meeting was held on October 25, 2012, which proposed a set of disease areas and requested public comment on them through a docket. The first 4 meetings were held on Chronic Fatigue Syndrome/ Myalgic Encephalomyelitis, HIV, Lung Cancer, and Narcolepsy. [illegible] Meeting links below. The regularly updated Schedule for future meetings (along with recordings from past meetings) can now be found at this link: http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm347317.htm	http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm347317.htm
6	I	100		PDUFA	XI B 4	By the end of FY 2017, FDA will conduct (or fund by contract) an assessment to evaluate the strengths, limitations, and the appropriate use of Sentinel for informing regulatory actions (e.g., labeling changes, PMRs and PMCs) to manage safety issues	Self-assessment	9/30/2017	9/30/2017	9/30/2017	CDER	Scheduled to begin after	–	N		http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm272170.htm
7	I	100		PDUFA	IX E 5	By the end of FY 2015, FDA will develop and implement staff training related to development, review and approval of drugs for rare diseases	Other	9/30/2015	9/30/2015	9/30/2015	CDER	Substantially complete, on track to meet due date	–	N		http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm272170.htm
8	I	100		PDUFA	XII G	FDA shall periodically publish final guidance specifying the completed data standards, formats, and terminologies that sponsors must use to submit data in applications.	Final Guidance	–	7/30/2014	7/30/2014	CDER	In process, on track to meet due date	–	Y		http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm272170.htm
9	I	100		PDUFA	XII F	To address FDA-identified nonclinical data standards needs, FDA will request public input on the use of relevant, already-existing data standards and the involvement of existing standards development organizations to develop new standards or refine existing standards. FDA will obtain this input via publication of a Federal Register notice that specifies a 60-day comment period	FR Notice	–	3/31/2014	3/31/2014	CDER	In process, on track to meet due date	–	Y		http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm272170.htm

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10	I	100		PDUFA	XII E 1	FDA shall develop a project plan for distinct therapeutic indications, prioritizing clinical efficiency standards development within and across review divisions. FDA shall publish a proposed project plan for stakeholder review and comment by June 30, 2013. FDA shall update and publish its project plan annually	Plan	6/30/2013	9/30/2013	10/23/2013	CDER	Completed	10/23/2013	Y	http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/ElectronicSubmissions/ucm287408.htm Open for public comment http://www.regulations.gov/#!documentDetail;D=FDA-2013-N-1277-0001 FR Notice posted. Public Meeting held on Nov 5, 2012 http://www.regulations.gov/#!documentDetail;D=FDA-2012-N-0750-0001 Meeting summary http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/ElectronicSubmissions/ucm332003.htm	http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/ElectronicSubmissions/ucm287408.htm
11	I	100		PDUFA	XII B	FDA will issue final guidance no later than 12 months from the close of the public comment period for the Draft eCTD Guidance on the standards and format of electronic submission of NDA, BLA and IND applications	Final Guidance	3/4/2014	9/30/2014	9/30/2014	CDER	In process, on track to meet due date	-	Y		http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm272170.htm
12	I	100		PDUFA	XII A	To enhance the quality and efficiency of FDA's review of NDAs, BLAs, and INDs, FDA shall consult with stakeholders, including pharmaceutical manufacturers and other research sponsors, to issue draft guidance on the standards and format of electronic submission of applications by December 31, 2012	Draft Guidance	12/31/2012	12/31/2012	12/31/2012	CDER	Completed	1/3/2013	Y	Completed 01/03/2013 http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM333969.pdf	http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM333969.pdf
13	I	100		PDUFA	XI B 2	By the end of FY 2015, FDA will conduct (or fund by contract) an interim assessment to evaluate the strengths, limitations and the appropriate use of Sentinel for informing regulatory actions (e.g., labeling changes, PMRs and PMCs) to manage safety issues	Self-assessment	9/30/2015	9/30/2015	9/30/2015	CDER	Scheduled to begin later	--	Y		http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm272173.htm
14	I	100		PDUFA	XI B 1	By the end of FY 2013, FDA will hold or support public meetings engaging stakeholders to discuss current and emerging Sentinel projects and facilitate stakeholder feedback and input regarding Sentinel projects that would be appropriate to meet the goals stated in the guidance	Public Meeting	9/30/2013	1/31/2013	1/31/2013	CDER	Completed	1/31/2013	Y	Completed Jan 31, 2013 http://www.brookings.edu/events/2013/01/31-sentinel-public-workshop	http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm272170.htm
15	I	100		PDUFA	XI A 3	FDA will issue guidance by the end of FY 2014 on methodologies for assessing a Risk Evaluation and Mitigation Strategy. This guidance should specifically address methodologies for determining whether a specific Risk Evaluation and Mitigation Strategy with elements to assure safe use (ETASU) is: (i) commensurate with the specific serious risk listed in the labeling of the drug and (ii) considering the observed risk, not unduly burdensome on patient access to the drug	Draft Guidance	9/30/2014	9/30/2014		CDER	In process, on track to meet due date	-	Y		http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm272170.htm

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16	I	100		PDUFA	XI A 3	By the end of FY 2013, FDA will initiate one or more public workshops on methodologies for assessing whether REMS are mitigating the risks they purport to mitigate and for assessing the effectiveness and impact of REMS, including methods for assessing the effect on patient access, individual practitioners, and the overall burden on the healthcare delivery system.	Public Meeting	9/30/2013	7/26/2013	7/26/2013	CDER	Completed	7/26/2013	Y	Completed 07/26/2013. FDA held a 2-day public meeting to obtain input on issues and challenges associated with the standardization and assessment of risk evaluation and mitigation strategies (REMS) for drug and biological products. The docket for written comments will remain open indefinitely. A link to the information can be found by following this link. http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm351029.htm	http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm351029.htm
17	I	100		PDUFA	XI A 2	To move towards increased integration of REMS into the healthcare delivery system, FDA will issue a report of its findings by the first quarter of FY 2014 that will identify at least one priority project in each of the following areas including a work plan for project completion: pharmacy systems, prescriber education, providing benefit/risk information to patients, and practice settings.	Public Report	12/31/2013	9/30/2014	3/31/2014	CDER	Scheduled to begin later	--	Y	Impacted by sequestration	http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm272170.htm
18	I	100		PDUFA	XI B 1	By the end of FY 2013, FDA will develop and issue guidance on how to apply the statutory criteria to determine whether a Risk Evaluation and Mitigation Strategy is necessary to ensure that the benefits of a drug outweigh the risks	Draft Guidance	9/30/2013	6/14/2014		CDER	In process on track to meet due date	--	Y		http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm272170.htm
19	I	100		PDUFA	X B	As appropriate, FDA will revise the CDER Clinical Review Template, Office and Division Director Summary Memo Templates, and corresponding Manuals of Policies and Procedures (MAPP) (and equivalent documents in CBER) to incorporate a structured benefit-risk assessment into the human drug review process on a timeframe outlined in the five-year plan referenced in Goal X.A.	SOP New Template				CDER	In process on track to meet due date	--	N	Revision will be made as appropriate.	http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm272170.htm
20	I	100		PDUFA	X A	By the end of the first quarter of 2013, FDA will publish for public comment its draft plan to further develop and implement a structured benefit-risk assessment in the new drug approval process	Plan	3/28/2013	3/29/2013	3/29/2013	CDER	Completed	3/5/2013	Y	Completed 03/05/2013. http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm326192.htm	http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm272170.htm
21	I	100		PDUFA	IX E 4	By the end of FY 2016, FDA, through the Rare Disease Program, will develop an evaluation tool to evaluate the success of the activities of the Rare Disease Program including the reviewer training	Other	9/30/2016	9/30/2016	9/30/2016	CDER	Scheduled to begin later	--	N		http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm272170.htm
22	I	100		PDUFA	IX E 1	By the end of FY 2013, FDA will complete a staffing and implementation plan for the CDER Rare Disease Program within the Office of New Drugs and a CBER Rare Disease liaison within the Office of Center Director	Plan	9/30/2013	9/30/2014	9/30/2014	CDER	In process on track to meet due date	--	N	Final Staffing and implement plan Staffing for CDER was Completed 12/12/2013 and Program is running	http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm272170.htm
23	I	100		PDUFA	IX D 2	By the end of FY 2014, FDA will hold a public meeting to discuss FDA's qualification standards for drug development tools, new measurement theory, and implications for multi-national trials.	Public Meeting	9/30/2014	9/30/2014	9/30/2014	CDER	Scheduled to begin later	--	Y		http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm272170.htm
24	I	100		PDUFA	IX C 3	By the end of FY 2013, FDA will hold a public meeting to discuss the current status of biomarkers and pharmacogenomics and potential strategies to facilitate scientific exchanges in regulatory and non-regulatory contexts	Public Meeting	9/30/2013	9/30/2014	9/30/2014	CDER	Scheduled to begin later	--	Y		http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm272170.htm

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25	I	100		PDUFA	IX.B.4 FDA will complete the final guidance describing FDA's intended approach to the use of meta-analyses in the FDA's regulatory review process (or revised draft guidance, if appropriate) within 3.5 years of the close of the public comment period for the draft guidance.	Final Guidance	-	6/30/2017	6/30/2017	CDER	Scheduled to begin later	-	N		http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm272170.htm
26	I	100		PDUFA	IX.B.3 Considering feedback and input received through a public meeting, FDA will publish draft guidance for comment describing FDA's intended approach to the use of meta-analyses in the FDA's regulatory review process by the end of FY 2015.	Draft Guidance	9/30/2015	9/30/2015	6/30/2015	CDER	In process, on track to meet due date	-	Y		http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm272170.htm
27	I	100		PDUFA	IX.B.1 FDA will develop a dedicated review team with appropriate expertise to evaluate different scientific methods and to explore the practical application of scientific approaches and best practices, including methodological limitations, for the conduct of meta-analyses in the context of FDA's regulatory review process.	Other	-	12/30/2015	12/30/2015	CDER	In process, on track to meet due date	-	N		http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm272170.htm
28	I	100		PDUFA	IX.A.2 FDA will publish final guidance (or revise draft guidance) for review staff and industry describing best practices for communication between FDA and IND sponsors during drug development), within 18 months of the close of the comment period for the draft guidance.	Final Guidance	12/31/2016	9/30/2016	6/30/2016	CDER	Scheduled to begin later	-	N		http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm272170.htm
29	I	100		PDUFA	IX.A.8 By the end of the second quarter of FY 2015, FDA will publish draft guidance for review staff and industry describing best practices for communication between FDA and IND sponsors during drug development.	Draft Guidance	3/31/2015	3/31/2015	3/31/2015	CDER	Scheduled to begin later	-	Y		http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm272170.htm
30	I	100		PDUFA	IX.A.7 By the end of FY 2014, the OND drug development and communication staff will provide training to all CDER staff involved in review of INDs.	Other	9/30/2014	9/30/2014	9/30/2014	CDER	In process, on track to meet due date	-	N		http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm272170.htm
31	I	100		PDUFA	IX.A.2 By the end of FY 2013, FDA will develop a dedicated drug development communication and training staff within the Office of New Drugs in CDER and augment the manufacturers assistance staff in CBER, focused on enhancing communication between FDA and sponsors during drug development.	SOP - New Template	9/30/2013	9/30/2014	9/30/2014	CDER	Scheduled to begin later	-	N		http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm272170.htm
32	I	100		PDUFA	II.B.2 FDA will hold a public meeting by no later than March 30, 2017, during which public stakeholders may present their views on the success of the new review program, including improving the efficiency and effectiveness of the first cycle review process and decreasing the number of review cycles ultimately necessary for new drugs and biologics that are approved.	Public Meeting	3/30/2017	3/30/2017	3/30/2017	CDER	Scheduled to begin later	-	Y		http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm272170.htm
33	I	100		PDUFA	II.B.2 A final assessment of the new review program will be published by December 31, 2016, for public comment.	Third Party Assessment	12/31/2016	12/31/2016	12/31/2016	CDER	Scheduled to begin later	-	Y		http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm272170.htm

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34	I	100		PDUFA	II.B.1	By June 30, 2015, FDA will hold a public meeting during which public stakeholders may present their views on the success of the new review program to date including: improving the efficiency and effectiveness of the first cycle review process, decreasing the number of review cycles ultimately necessary for new drugs and biologics that are approved, and helping to ensure that patients have timely access to safe, effective, and high quality new drugs and biologics.	Public Meeting	6/30/2015	6/30/2015	6/30/2015	CDER	Scheduled to begin later	–	Y		http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm272170.htm
35	I	100		PDUFA	II.B.1	An interim assessment of the new program for enhanced review transparency and communication for new molecular entity NDAs and original BLAs ("new review program") will be published by March 31, 2015, for public comment	Third Party Assessment	3/31/2015	3/30/2015	3/30/2015	CDER	Scheduled to begin later	–	Y		http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm272170.htm
36	I	100		PDUFA	II.B	The new review program for new molecular entity NDAs and original BLAs shall be evaluated by an independent contractor with expertise in assessing the quality and efficiency of biopharmaceutical development and regulatory review programs. The statement of work for this effort will be published for public comment prior to beginning the assessment. The assessments will occur continuously throughout the course of the new review program.	FR Notice	–	–	7/9/2012	CDER	Completed	7/9/2012	Y		http://www.gpo.gov/fdsys/pkg/FR-2012-07-09/pdf/2012-16639.pdf
37	I	100		PDUFA	II.A	FDA will establish a new review model that will apply to all New Molecular Entity New Drug Applications (NME NDAs) and original Biologics License Applications (BLAs), including applications that are resubmitted following a Refuse-to-File action, received from October 1, 2012, through September 30, 2017	SOP / New Template	–	10/1/2012	10/1/2012	CDER	Completed	10/1/2012	N		http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm272170.htm
38	I	103	(2)(a)	NO		FDA shall determine the inflation and workload adjustments for PDUFA and publish them in the Federal Register	FR Notice	8/2/2012	8/3/2012	8/2/2012	OFM	Completed	8/1/2012	Y	8/1/2012 Completed http://www.gpo.gov/fdsys/pkg/FR-2012-08-01/pdf/2012-18711.pdf	David Miller David.Miller@fda.hhs.gov
39	I	103	(2)(a)	NO		FDA shall contract with an independent accounting or consulting firm to periodically review the adequacy of the workload adjustment for PDUFA and publish the results of those reviews for public comment. The first review, due at the end of FY 2013, is to examine the performance of the adjustment since fiscal year 2009	Public Report	9/30/2013	9/30/2013	9/30/2013	OPL	Completed	5/6/2013	Y	Completed 05/06/2013 http://www.fda.gov/downloads/ForIndustry/UserFees/PrescriptionDrugUserFee/UCM350567.pdf	Giles Mills giles.mills@fda.hhs.gov
40	I	103	(2)(a)	NO		FDA shall establish fees for PDUFA and publish the fees, and rationale for any adjustments, in an FR notice	FR Notice	8/2/2012	8/3/2012	8/3/2012	OFM	Completed	8/1/2012	Y	8/1/2012 Completed http://www.gpo.gov/fdsys/pkg/FR-2012-08-01/pdf/2012-18711.pdf	David Miller David.Miller@fda.hhs.gov
41	I	103	(2)(b)	NO		FDA shall contract with an independent accounting or consulting firm to periodically review the adequacy of the PDUFA workload adjustment and publish the results of these reviews for public comment. The second review, due at the end of FY 2015, is to examine the continued performance of the adjustment.	Public Report	9/30/2015	9/30/2015	9/30/2015	OPL	Scheduled to begin later	–	Y		Giles Mills giles.mills@fda.hhs.gov
42	I	104		NO		FDA shall submit to Congress an annual Performance Report for PDUFA	Report to Congress	1/28/2014	1/28/2014	12/31/2013	OPL	Completed	1/31/2014	Y	Completed 1/31/2014 http://www.fda.gov/AboutFDA/ReportsManualsForms/Reports/UserFeeReports/PerformanceReports/PDUFA/ucm384028.htm	http://www.fda.gov/AboutFDA/ReportsManualsForms/Reports/UserFeeReports/PerformanceReports/default.htm

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Item #	Title	Section *	Sub-Section	UFA Goals Letter	Goals Letter Citation	Deliverable Description	Deliverable Type	Statutory Deadline *	Targeted Completion Date **	FDA Completion Due Date **	Responsible Organization	Status ***	Date Completed	Publicly Tracked? (FDASIA-TRACK)	FDASIA TRACK Notes (Will be posted on public FDA-TRACK Website)	Public Website Contact
43	II	200		MDUFA	II.D.1b*	FDA will update its website to reflect the following: 1. A list of premarket device guidance documents (an "A-list") that the Agency intends to publish within 12 months of the date the list is published each fiscal year, and 2. A list of device guidance documents (a "B-list") that the Agency intends to publish, as the Agency's guidance development resources permit each fiscal year	FR Notice	--	1/1/2013	1/1/2013	CDRH	Completed	--	Y		CDRH-FDASIA@fda.hhs.gov
44	II	200		MDUFA	II.D.1a	FDA will update its website in a timely manner to reflect the following:1. The Agency's review of previously published device guidance documents, including the deletion of guidance documents that no longer represent the Agency's interpretation of, or policy on, a regulatory issue, and notices of guidance documents that are under review by the Agency.	FR Notice	--	11/23/2012	11/23/2012	CDRH	In process on track to meet due date	--	N		CDRH-FDASIA@fda.hhs.gov
45	II	200		MDUFA	II.C	FDA will update the interactive review guidance to enhance the interactive review process between FDA and applicants to facilitate timely completion of premarket reviews, based on accurate and complete [illegible] of	Final Guidance	--	9/1/2013	9/1/2013	CDRH	Undergoing FDA Clearance	--	Y	-- Completed 12/31/2012 http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM313794.pdf	CDRH-FDASIA@fda.hhs.gov
46	II	200		MDUFA	II.B	FDA will publish final guidance outlining electronic copy of submissions (eCopy)	Final Guidance	--	1/1/2013	1/1/2013	CDRH	Completed	12/31/2012	Y		CDRH-FDASIA@fda.hhs.gov
47	II	200		MDUFA	II.B	FDA will publish draft guidance outlining electronic copy of submissions (eCopy)	Draft Guidance	--	10/1/2012	10/1/2012	CDRH	Completed	10/17/2012	Y	Completed 10/17/2012	CDRH-FDASIA@fda.hhs.gov
48	II	200		MDUFA	II.A	FDA will issue guidance on a structured process for managing Pre-Submission (draft) guidance issued on or [illegible]	Final Guidance	--	2/4/2014	2/4/2014	CDRH	Undergoing FDA Clearance	--	Y		CDRH-FDASIA@fda.hhs.gov
49	II	200		MDUFA	II.E	FDA will issue guidance regarding the review and management expectations for Clinical Laboratory Improvement Amendment waivers throughout the entire submission process	Draft Guidance	--	3/31/2014	3/31/2014	CDRH	In process, on track to meet due date	--	Y		CDRH-FDASIA@fda.hhs.gov
50	II	200		MDUFA	V	After the completion of the 3rd party assessment and issuance of the GRMP guidance, FDA's implementation of the GRMP guidance will include initial and ongoing training of FDA staff, and periodic audits of compliance with the guidance	SOP / New Template	--	2/1/2017	2/1/2017	CDRH	Scheduled to begin later	--	N		CDRH-FDASIA@fda.hhs.gov
51	II	200		MDUFA	V	After the completion of the 3rd party assessment, FDA will solicit public comments on the Good Review Management Practices (GRMP) draft guidance document and then finalize the guidance document	Final Guidance	--	2/1/2017	2/1/2017	CDRH	Scheduled to begin later	--	Y		CDRH-FDASIA@fda.hhs.gov
52	II	200		MDUFA	V	After the completion of Phase 1 of the 3rd party assessment, FDA will incorporate the results of the independent assessment of the review process for device submissions into a Good Review Management Practices (GRMP) draft guidance document	Draft Guidance	--	9/30/2015	9/30/2015	CDRH	Scheduled to begin later	--	Y		CDRH-FDASIA@fda.hhs.gov
53	II	200		MDUFA	V	FDA will analyze the recommendations for improvement opportunities identified in the assessment, develop and implement a corrective action plan, and assure its effectiveness	Plan	--	9/30/2016	9/30/2016	CDRH	Scheduled to begin later	--	N		CDRH-FDASIA@fda.hhs.gov
54	II	200		MDUFA	V	For Phase 2 of the assessment, the contractor will evaluate the implementation of recommendations and publish a written assessment no later than February 1, 2016	Third Party Assessment	2/1/2016	2/1/2016		CDRH	Scheduled to begin later		Y		CDRH-FDASIA@fda.hhs.gov

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Item #	Title	Section *	Sub-Section	UFA Goals Letter	Goals Letter Citation	Deliverable Description	Deliverable Type	Statutory Deadline *	Targeted Completion Date **	FDA Completion Due Date **	Responsible Organization	Status ***	Date Completed	Publicly Tracked (FD ASIA-TRACK)	FDASIA TRACK Notes (Will be posted on public FDA TRACK Website)	Public Website Contact
55	II	200		MDUFA	V	FDA will publish an implementation plan within 5 months of receipt of the final recommendations from the independent assessment.	Plan	-	12/11/2014	12/11/2014	CDRH	Scheduled to begin later	-	Y		CDRH-FDASIA@fda.hhs.gov
56	II	200		MDUFA	V	FDA will publish an implementation plan based on the independent assessment's set of high-priority recommendations within 6 months of receipt	Plan	-	6/11/2013	6/11/2013	CDRH	In process, on track to meet due date	-	Y		CDRH-FDASIA@fda.hhs.gov
57	II	200		MDUFA	V	The final comprehensive findings and recommendations from the independent assessment will be published within 1 year of contract award	Third Party Assessment	-	6/11/2014	6/11/2014	CDRH	In process, on track to meet due date	-	Y		CDRH-FDASIA@fda.hhs.gov
58	III	200		MDUFA	V	Findings on high-priority recommendations from the independent assessment will be published within six months of awarding the contract.	Third Party Assessment	12/15/2013	9/30/2013		CDRH	Completed	12/11/2013	Y	http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/OverviewMedicalDevices/UCM382802.pdf	CDRH-FDASIA@fda.hhs.gov
59	V	200		MDUFA	V	FDA and the device industry will participate in a comprehensive two-phase assessment of the process for the review of device applications. For Phase 1, no later than the end of the second quarter of FY 2013 FDA will contract with a private, independent consulting firm capable of performing the technical analysis, management assessment, and program evaluation tasks required to address the assessment accep	Other	3/31/2013	5/30/2013		CDRH	Completed	6/12/2013	Y		CDRH-FDASIA@fda.hhs.gov
60	V	200		MDUFA	IV B i b i	FDA will hold a minimum of two medical device Vendor Days each year.	Other	9/30/2013	9/30/2013	5/20/2013	CDRH	Completed	5/22/2013	Y		CDRH-FDASIA@fda.hhs.gov
61	II	200		MDUFA	IV B	FDA will implement its Reviewer Certification Program for CDRH reviewers and publish the curriculum in this program and other course offerings. FDA will consider comments from stakeholders when making updates to courses and determining course offerings	List	-	9/30/2013		CDRH	Completed	9/30/2013	N	http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/OverviewMedicalDeviceUserFeeandModernizationAct/MDUFMAUcm305210.htm	CDRH-FDASIA@fda.hhs.gov
62	II	200		MDUFA	IV A	During MDUFA III, FDA will also work with industry to benchmark best practices for retaining employees (both financial and non-financial)	Plan		12/31/2014	12/31/2013	CDRH	In process, on track to meet due date	-	N		CDRH-FDASIA@fda.hhs.gov
63	II	200		MDUFA	II D	FDA will issue guidance providing objective criteria for making decisions to accept or refuse to accept 510(k) premarket notifications for review	Final Guidance	-	9/30/2013	9/30/2013	CDRH	Completed	12/31/2012	Y		CDRH-FDASIA@fda.hhs.gov
64	II	200		MDUFA	II A	FDA will issue guidance providing objective criteria for making decisions to accept or refuse to accept premarket approval applications for review	Final Guidance	-	9/30/2013	9/30/2013	CDRH	Completed	12/31/2012	Y		CDRH-FDASIA@fda.hhs.gov
65	II	200		MDUFA	II G	By the end of FY 2015, FDA intends to issue a final rule exempting additional low risk medical devices from premarket notification	Final Guidance	9/30/2015	9/30/2015	9/30/2015	CDRH	Scheduled to begin after Undergoing FDA Clearance	-	Y		CDRH-FDASIA@fda.hhs.gov
66	II	200		MDUFA	II G	By the end of FY 2013, FDA intends to develop a draft list of low risk medical devices that will be considered for exemption from premarket notification	Draft Guidance	9/30/2013	9/30/2014		CDRH		-	Y		CDRH-FDASIA@fda.hhs.gov

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FOOD AND DRUG SAFETY AND INNOVATION ACT (FDASIA) INTERNAL TRACKING SHEET

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Item #	Title	Section *	Sub-Section	UFA Goals Letter	Goals Letter Citation	Deliverable Description	Deliverable Type	Statutory Deadline *	Targeted Completion Date **	FDA Completion Due Date **	Responsible Organization	Status ***	Date Completed	Publicly Tracked? (FDASIA-TRACK)	FDASIA TRACK Notes (Will be posted on public FDA-TRACK Website)	Public Website Contact
67	II	200	—	MDUFA	I.F	Over the period of MDUFA III, FDA will meet with patient groups to better understand and characterize the patient perspective on disease severity or unmet medical need. In addition, FDA will increase its utilization of FDA's Patient Representatives as Special Government Employee consultants to CDRH to provide patients' views early in the medical product development process and ensure those perspectives are considered in regulatory discussions. Applicable procedures governing conflicts of interest and confidentiality of proprietary information will be utilized for these consultations.	Public Meeting	—	9/30/2013	9/30/2013	CDRH	completed	9/18/2013	N		CDRH-FDASIA@fda.hhs.gov
68	II	200		MDUFA	I.O	FDA will establish a process allowing stakeholders an opportunity to 1. Provide meaningful comments and/or propose draft language for proposed guidance topics in the "A" and "B" lists, 2. Provide suggestions for new or different guidance documents, and 3. Comment on the relative priority of topics for guidance.	FR Notice	—	11/23/2012	11/23/2012	CDRH	Completed	—	N		CDRH-FDASIA@fda.hhs.gov
69	II	200		MDUFA		FDA will update the interactive review guidance to enhance the interactive review process between FDA and applicants to facilitate timely completion of premarket reviews based on accurate and complete information.	Draft Guidance	—	3/5/2013	3/5/2013	CDRH	Completed	3/5/2013	Y	Completed January 2013 http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Overview/MDUFA/ucm321367.htm	
70	II	203	(a)(4)	NC		FDA shall establish fees for MDUFA and publish the fees and rationale for any adjustments in an FR notice	FR Notice	8/2/2012	8/3/2012	8/3/2012	OFM	Completed	7/31/2012	Y	Completed 7/31/2012 http://www.gpo.gov/fdsys/pkg/FR-2012-07-31/html/2012-18547.htm	David Miller David.Miller@fda.hhs.gov or http://www.fda.gov/AboutFDA/ReportsManualsForms/Reports/UserFeeReports/PerformanceReports/default.htm
71	II	204	(b)	NC		FDA shall submit to Congress an annual Performance Report for MDUFA	Report to Congress		1/28/2014	12/31/2013	OPL	Completed	1/31/2014	Y	Completed 1.31.2014 http://www.fda.gov/AboutFDA/ReportsManualsForms/Reports/UserFeeReports/PerformanceReports/MDUFMA/ucm353986.htm	http://www.fda.gov/AboutFDA/ReportsManualsForms/Reports/UserFeeReports/PerformanceReports/default.htm
72	II	204	(b)	NC		FDA shall make the annual Performance Report available on the FDA website	Public Report	1/28/2014	1/28/2014	1/28/2014	OPL	Completed	1/31/2014	N	Completed 1.31.2014 http://www.fda.gov/AboutFDA/ReportsManualsForms/Reports/UserFeeReports/PerformanceReports/MDUFMA/ucm383983.htm	http://www.fda.gov/AboutFDA/ReportsManualsForms/Reports/UserFeeReports/PerformanceReports/default.htm
73	II	204	(b)	NC		FDA shall make MDUFA quarterly performance data publicly available on the FDA website	Public Report	3/1/2013	3/1/2013	3/1/2013	CDRH	Completed	2/12/2013	Y	Completed 2/12/2013 http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/Overview/MedicalDeviceUserFeeandModernizationAct/MDUFMA/UCM339968.pdf	http://www.fda.gov/AboutFDA/ReportsManualsForms/Reports/UserFeeReports/PerformanceReports/default.htm
74	II	208		MDUFA	IV.A	FDA may hire employees for activities related to the process for the review of device applications outside of the competitive service provisions of the federal civil service for 5 years after the date of enactment. The FDA shall institute appropriate internal controls for appointments under this section.	Plan	—	10/1/2012		CDRH	Completed	—	N		

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75	III	300		GDUFA	3 C	To maximize the number of applications that can be reviewed within the review goals and to assist in securing the pharmaceutical supply chain, FDA will employ a risk-based biennial CGMP surveillance inspection model for inspection of generic API and FDF manufacturers, with the goal of achieving parity of inspection frequency between foreign and domestic establishments in FY 2017 and will prioritize inspections of establishments associated with ANDAs that are otherwise approvable or eligible for tentative approval except for an outstanding inspection, as well as establishments that have not been inspected previously	Other	--	--		ORA	Completed	--	N	--	www.fda.gov/gdufa AskGDUFA@fda.hhs.gov
76	III	300		GDUFA	4 D	FDA will conduct risk-adjusted biennial CGMP surveillance inspections of generic API and generic finished dosage form (FDF) manufacturers, with the goal of achieving parity of inspection frequency between foreign and domestic firms in FY 2017	Other	9-30-2017			CDER	Scheduled to begin later	-	N		www.fda.gov/gdufa AskGDUFA@fda.hhs.gov
77	III	300		GDUFA	4 A	FDA will hire and train at least 25 percent of incremental staff in FY 2013, 50 percent in FY 2014 and will strive to complete GDUFA-funded human resources hiring goals in FY 2015 as necessary to achieve the program's performance metrics and goals	Other	--	9-30-2013	9-4-2013	CDER	Completed	9-4-2013	N		www.fda.gov/gdufa AskGDUFA@fda.hhs.gov
78	III	300		GDUFA	3.B	FDA will solicit input from industry and other stakeholders to develop an annual list of regulatory science initiatives	List	--			CDER	Completed		N	Annual process Regulatory Research Results for FY 2013 have been posted as well as Project Continuation in the FY14 priorities. Information regarding these efforts can be found http://www.fda.gov/Drugs/NewsEvents/ucm367997.htm	www.fda.gov/gdufa AskGDUFA@fda.hhs.gov
79	III	300		GDUFA	3.A	FDA will convene a working group and consider suggestions from industry and other stakeholders to develop an annual list of regulatory science initiatives for review by CDER Director	Public Meeting	--	6/21/2013	6/21/2013	CDER	Completed	6/21/2013	N	Annual process June 21, 2013 public meeting held and comments submitted to a public docket. Regulatory Research Results for FY 2013 have been posted as well as Project Continuation in the FY14 priorities. Information regarding these efforts can be found http://www.fda.gov/Drugs/NewsEvents/ucm367997.htm	www.fda.gov/gdufa AskGDUFA@fda.hhs.gov
80	III	300		GDUFA	3.D	FDA will develop a current chemistry, manufacturing and controls (CMC) records database to aid in the efficiency of review and inspection	Database/IT System	--	--		CDER	In process on track to meet due date	--	N		www.fda.gov/gdufa AskGDUFA@fda.hhs.gov

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Item #	Title	Section *	Sub-Section	LFA Goals Letter	Goals Letter Citation	Deliverable Description	Deliverable Type	Statutory Deadline *	Targeted Completion Date **	FDA Completion Due Date **	Responsible Organization	Status ***	Date Completed	Publicly Tracked?(FDASIA TRACK)	FDASIA TRACK Notes (will be posted on public FDA TRACK Website)	Public Website Contact *
81	III	300		GDUFA	2 D	FDA will develop new and/or enhance existing facility databases (API and FDF manufacturing and clinical bioequivalence site) to be populated by industry. These databases will, at a minimum, contain information for generics-related firms, including addresses and Data Universal Numbering System (DUNS) numbers, and will link facilities to DMFs and ANDAs, and will contain other information as necessary.	Database/IT System	--	9/30/2013	9/28/2013	CDER	Completed	9/28/2013	Y	Completed 09/28/2013	www.fda.gov/gdufa Ask.GDUFA@fda.hhs.gov
82	III	300		GDUFA	2 D	During the five years of the program, FDA will undertake a study of foreign government regulatory inspections (CGMP and bioequivalence), report findings publicly, and develop a program to utilize foreign inspection classifications when and where appropriate.	Other	--	9/30/2017		CDER	Scheduled to begin later	--	Y		www.fda.gov/gdufa Ask.GDUFA@fda.hhs.gov
83	III	300		GDUFA	2 C	FDA will make inspection classification results and data of the last facility inspection available to the public and update on FDA's website on a timely basis.	Public Report	--	10/1/2012		CDER	Completed	10/2/2012	Y	http://www.accessdata.fda.gov/scripts/inspsearch	www.fda.gov/gdufa Ask.GDUFA@fda.hhs.gov
84	III	302		NO		FDA will publish in the Federal Register the one-time backlog fee for accepted new drug applications (ANDAs) that are pending on October 1, 2012, and that have not received a tentative approval prior to that date. (GDUFA Fee)	FR Notice	10/31/2012	10/31/2012	10/31/2012	OFM	Completed	10/25/2012	Y	Action Completed October 25, 2012 http://www.gpo.gov/fdsys/pkg/FR-2012-10-25/pdf/2012-26257.pdf	http://www.fda.gov/ForIndustry/UserFees/GenericDrugUserFees/ucm322829.htm http://www.fda.gov/ForIndustry/UserFees/GenericDrugUserFees/ucm322829.htm
85	III	302		NO		FDA shall establish fees for GDUFA (drug master file fees and 6 reg fees) and publish the fees in an FR notice.	FR Notice	10/31/2012	10/31/2012	10/31/2012	OFM	Completed	10/25/2012	Y	Action Completed October 25, 2013 http://www.gpo.gov/fdsys/pkg/FR-2012-10-25/pdf/2012-26256.pdf	http://www.fda.gov/ForIndustry/UserFees/GenericDrugUserFees/ucm322829.htm
86	III	302		NO		FDA will establish generic drug user fee rates (GDUFA) for domestic and foreign active pharmaceutical ingredient (API) and finished dosage format (FDF) facilities and publish the fees in an FR notice. FDA will publish in the Federal Register a notice requiring each person that owns certain specified facilities or organizations to submit to FDA information on the identity of each such facility, site, or organization. The facilities and organizations specified are those that: produce one or more finished dosage forms of a human generic drug or an active pharmaceutical ingredient (API) contained in a finished generic drug, or a site or organization in which a bioanalytical study is conducted, a clinical research organization, a contract analytical testing site, or a [illegible]	FR Notice	1/14/2013	1/15/2013	1/15/2013	OFM	Completed	1/17/2013	Y	Completed January 17, 2013 http://www.gpo.gov/fdsys/pkg/FR-2013-01-17/pdf/2013-00951.pdf	http://www.fda.gov/ForIndustry/UserFees/GenericDrugUserFees/ucm322829.htm
87	III	302		NO		The facilities shall assess and collect fees in accordance with this section one-time backlog fee, drug master file fee, abbreviated new drug application and prior approval supplement filing fee, generic drug facility fee and active pharmaceutical ingredient facility fee.	FR Notice	10/1/2012	10/1/2012	10/1/2012	CDER	Completed	10/1/2012	Y	Completed http://www.gpo.gov/fdsys/pkg/FR-2012-10-02.pdf/2012-24316.pdf	www.fda.gov/gdufa Ask.GDUFA@fda.hhs.gov
88	III	302		NO			Other	10/1/2012	10/1/2012	10/1/2012	OFM	Completed	10/1/2012	N	Action completed http://www.fda.gov/ForIndustry/UserFees/GenericDrugUserFees/ucm322829.htm	http://www.fda.gov/ForIndustry/UserFees/GenericDrugUserFees/ucm322829.htm http://www.fda.gov/ForIndustry/UserFees/GenericDrugUserFees/ucm322829.htm
89	III	302		NO		FDA shall publish in the Federal Register the amount of the GDUFA inflation adjustment.	FR Notice	10/31/2013	11/1/2013	11/1/2013	OFM	Scheduled to begin later	--	N		http://www.fda.gov/ForIndustry/UserFees/GenericDrugUserFees/ucm322829.htm

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90	III	302		NO		FDA shall make available on its Web site a list of DMF numbers for DMFs that have undergone an initial completeness assessment and are available for reference	Website	–	–		CDER	Completed	12/19/2012	Y	Action Completed 12/19/2012 http://www.fda.gov/downloads/ForIndustry/UserFees/GenericDrugUserFees/UCM332875.pdf	www.fda.gov/gdufa AskGDUFA@fda.hhs.gov
91	III	303		NO		FDA shall submit to Congress an annual Performance Report for all generic drug applications, amendments and prior approval supplements, that includes the number of applications that met the GDUFA goals, the average total time to decision, including the number of calendar days spent during FDA review and calendar days taken by sponsor, total number of applications that were pending for more than 10 months on July 9, 2012, and the number of pending applications on which FDA took final regulatory action in the previous fiscal year	Report to Congress	1/25/2014	1/25/2014	12/31/2013	OPL	Completed	1/31/2014	Y	Completed 1-31-2014 http://www.fda.gov/AboutFDA/ReportsManualsForms/Reports/UserFeeReports/PerformanceReports/ucm384247.htm	http://www.fda.gov/AboutFDA/ReportsManualsForms/Reports/UserFeeReports/PerformanceReports/default.htm
92	III	303		NO		FDA shall submit to Congress an annual Fiscal Report for GDUFA.	Report to Congress	1/28/2014	1/28/2014	1/28/2014	OFM	Completed	4/30/2014	Y	Completed 4-30-2014 http://www.fda.gov/AboutFDA/ReportsManualsForms/Reports/UserFeeReports/FinancialReports/GDUFA/ucm395903.htm	http://www.fda.gov/ForIndustry/UserFees/GenericDrugUserFees/ucm322629.htm
93	III	303		NO		FDA shall submit recommendations to Congress for generic drug user fee reauthorization	Report to Congress	1/15/2017	10/15/2016	10/1/2016	CDER	Scheduled to begin later	–	Y		www.fda.gov/gdufa AskGDUFA@fda.hhs.gov
94	III	303		NO		FDA shall present recommendations to Congress on GDUFA reauthorization, publish in Federal Register and provide a 30 day comment period for the public, hold a public meeting on recommendations, and after consideration of public views, revise such recommendations	Public Meeting	1/13/2017	10/31/2016	10/15/2016	CDER	Scheduled to begin later	–	N		www.fda.gov/gdufa AskGDUFA@fda.hhs.gov
95	III	303		NO		Prior to beginning negotiations with the generic industry concerning extension of generic drug user fees beyond Fiscal Year 2017, FDA shall consult with stakeholders	FR Notice	–	4/1/2015	3/15/2015	CDER	Scheduled to begin later	–	Y		www.fda.gov/gdufa AskGDUFA@fda.hhs.gov
96	III	303		NO		FDA shall make the annual GDUFA performance report available on FDA website	Public Report	–	2/28/2014	2/25/2014	OPL	Completed	1/31/2014	N	Completed 1-31-2014 http://www.fda.gov/AboutFDA/ReportsManualsForms/Reports/UserFeeReports/PerformanceReports/ucm384247.htm	http://www.fda.gov/AboutFDA/ReportsManualsForms/Reports/UserFeeReports/PerformanceReports/GDUFA/default.htm
97	III	303		NO		FDA shall make the annual GDUFA fiscal report available on FDA website	Public Report	–	2/28/2014	2/28/2014	OFM	Completed	4/30/2014	Y	Completed 4/30/2014 http://www.fda.gov/AboutFDA/ReportsManualsForms/Reports/UserFeeReports/FinancialReports/GDUFA/ucm395903.htm	http://www.fda.gov/ForIndustry/UserFees/GenericDrugUserFees/ucm322629.htm
98	III	303		NO		FDA shall make minutes of GDUFA negotiation meetings available on the FDA website	Public Report	2/13/2017	2/13/2017	2/13/2017	CDER	Scheduled to begin later	–	N		www.fda.gov/gdufa AskGDUFA@fda.hhs.gov
99	IV	402		NO		FDA shall establish Initial Biosimilar Biological Product Development Fee, Annual Biosimilar Biological Product Development Fee, Reactivation Fee, Biosimilar Biological Product Application Fee, Establishment Fee and Product Fee and publish fees in an FR notice	FR Notice	8/1/2012	8/1/2012	3/1/2012	OFM	Completed	8/1/2012	Y	Completed August 1, 2012 http://www.gpo.gov/fdsys/pkg/FR-2012-08-01/pdf/2012-18712.pdf	http://www.gpo.gov/fdsys/pkg/FR-2012-08-01/pdf/2012-18712.pdf
100	IV	402		NO		FDA shall collect fees from industry to support the Agency's biosimilar biological product review activities under a new biosimilar user fee program from FY2013 through FY2017. Fee amounts are based on adjusted PDUFA fee amounts for each fiscal year	Other	10/1/2012	10/1/2012	10/1/2012	OFM	Completed	–	N		http://www.fda.gov/ForIndustry/UserFees/BiosimilarUserFeeActBsUFA/ucm320768.htm

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FOOD AND DRUG SAFETY AND INNOVATION ACT (FDASIA) INTERNAL TRACKING SHEET

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Item #	Title	Section *	Sub-Section	UFA Goals Letter	Goals Letter Citation	Deliverable Description	Deliverable Type	Statutory Deadline *	Targeted Completion Date **	FDA Completion Due Date **	Responsible Organization	Status ***	Date Completed	Publicly Tracked? (FDASIA-TRACK)	FDASIA TRACK Notes (Will be posted on public FDA-TRACK Website)	Public Website Contact
101	IV	403	(d)	NO		FDA shall contract with independent accounting or consulting firm to study the workload volume and full costs associated with the process for review of biosimilar biological product applications, and publish, for public comment, interim results of the study	Third Party Assessment	6/1/2015	6/1/2015		CDER	Scheduled to begin later	-	Y		druginfo@fda.hhs.gov
102	IV	403	(d)	NO		FDA shall contract with independent accounting or consulting firm to study the workload volume and full costs associated with the process for review of biosimilar biological product applications, and publish for public comment, final results of the study	Third Party Assessment	9/29/2016	9/29/2016		CDER	Scheduled to begin later	-	Y		druginfo@fda.hhs.gov
103	IV	402	(a)(1)	NO		FDA shall consult with stakeholders and publish an FR notice requesting public input on recommendations for biosimilar user fee program reauthorization, shall hold a public meeting, solicit comments, and publish comments on the FDA website	Public Meeting	1/13/2017	10/15/2016		CDER	Scheduled to begin later	-	N		druginfo@fda.hhs.gov
104	IV	405	(e)(3)	NO		FDA shall submit recommendations to Congress for biosimilar user fee program reauthorization	Report to Congress	1/13/2017	1/13/2017		CDER	Scheduled to begin later	-	Y		druginfo@fda.hhs.gov
105	IV	403		NO		FDA shall submit to Congress an annual Fiscal Report for BSUFA	Report to Congress	1/25/2014	1/28/2014	1/28/2014	OFM	Scheduled to begin later	-	Y		http://www.fda.gov/ForIndustry/UserFees/GenericDrugUserFees/ucm322629.htm
106	IV	403		NO		FDA shall submit to Congress an annual Performance Report for BSUFA	Report to Congress	1/28/2014	1/28/2014	12/31/2013	OPL	Completed	1/31/2014	Y	Completed 1/31/2014 http://www.fda.gov/AboutFDA/ReportsManualsForms/Reports/UserFeeReports/PerformanceReports/MDUFMA/ucm323988.htm	http://www.fda.gov/AboutFDA/ReportsManualsForms/Reports/UserFeeReports/PerformanceReports/default.htm
107	IV	403		NO		FDA shall make annual BSUFA fiscal report available on the FDA website	Public Report	-	1/28/2014	1/28/2014	OFM	Completed	4/30/2014	Y	Completed 4/30 2014 http://www.fda.gov/AboutFDA/ReportsManualsForms/Reports/UserFeeReports/FinancialReports/BsUFA/ucm325672.htm	http://www.fda.gov/ForIndustry/UserFees/BiosimilarUserFeeActBsUF A/ucm320782.htm
108	IV	403		NO		FDA shall make the annual BSUFA performance report available on the FDA website	Public Report	-	2/28/2014	2/28/2014	OPL	Completed	1/31/2014	N	Completed 1/31/2014 http://www.fda.gov/AboutFDA/ReportsManualsForms/Reports/UserFeeReports/PerformanceReports/MDUFMA/ucm383968.htm	http://www.fda.gov/AboutFDA/ReportsManualsForms/Reports/UserFeeReports/PerformanceReports/default.htm
109	IV	406		NO		FDA shall submit to Congress an annual report that includes the number of biosimilar applications filed, the percentage of filed biosimilar applications that were approved and an explanation of how FDA is managing the biosimilar review program to ensure that PDUFA funds are not being used to support the review of biosimilar applications	Report to Congress	1/28/2015	1/28/2015	1/28/2015	OPL	Scheduled to begin later	-	Y		http://www.fda.gov/AboutFDA/ReportsManualsForms/Reports/UserFeeReports/PerformanceReports/default.htm
110	V	502	(b)	NO		FDA must describe the rationale for not requesting studies in neonates in written requests	Other	7/9/2012	7/9/2012	7/9/2012	CDER	Completed	7/9/2012	N		pdit@fda.hhs.gov

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FOOD AND DRUG SAFETY AND INNOVATION ACT (FDASIA) INTERNAL TRACKING SHEET

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111	V	503		NO		FDA shall issue internal standard operating procedures for any significant modifications to initial pediatric study plans, agreed initial pediatric study plans, and written requests. Such operating procedures shall be posted to FDA's website.	SOP / New Template	7/9/2013	7/9/2013	7/9/2013	CDER	Completed	6/25/2013	Y	Below is a link to a presentation recently presented to industry outlining how to apply the new pediatric laws to current drug development including the recent modifications to initial pediatric study plans. http://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/DevelopmentResources/UCM355309.pdf Additionally, an outline of procedures and timelines for review of PSPs and Written Requests by the Pediatric Review Committee can be found by this link: http://inside.fda.gov:9003/downloads/CDER/OfficeofNewDrugs/ImmediateOffice/PediatricandMaternalHealthStaff/UCM353955.pdf	pdit@fda.hhs.gov
112	V	504		NO		Not later than 3 years after the date of enactment of FDASIA, FDA shall post to FDA's website medical, statistical, and clinical pharmacology reviews of pediatric studies under 505A(b) or (c) submitted between 01/04/2002 and 09/27/2007 for which 6 months of exclusivity was granted & that resulted in a labeling change.	Other	7/9/2015	7/9/2015	7/9/2015	CDER	Scheduled to begin later	-	N		pdit@fda.hhs.gov
113	V	505	(a)(4)(B)	NO		New procedure for deferrals, deferral extensions, and reporting. For a deferral that expired prior to the date of enactment or that expired prior to 270 days after the date of enactment and for which a deferral extension request was submitted no later than 180 days after enactment (January 5, 2013), response by FDA due 1 year after enactment. FDA shall make certain information from annual review of deferred studies information publicly available on the FDA website.	SOP / New Template	7/9/2013	--	1/5/2013	CDER	Completed	1/5/2013	N	Completed. Process for reviewing and granting Deferral Extensions implemented	http://inside.fda.gov:9003/CDER/OfficeofNewDrugs/ImmediateOffice/PediatricandMaternalHealthStaff/ucm027529.htm
114	V	505	(b)	NO		Amends FD&C Act Section 505B(f)(6)(D) to require tracking and aggregation on an annual basis of the total number of deferrals/deferral extensions requested and granted pursuant to 505B of the FDCA and the reasons for deferral/deferral extensions, the timeline for completion of assessments and the number of assessments complete	Public Report				CDER	In process on track to meet due date	-	N		pdit@fda.hhs.gov
115	V	505	(c)	NO		Beginning 270 days after enactment, FDA shall issue non-compliance letter informing of failure to submit assessments pursuant to or meet certain requirements of 505B of FDCA; letter shall require response within 45 calendar days of issuance; Requires posting of non-compliance letters and responses; Requires tracking of the number of postmarket non-compliance letters issued pursuant to 505B of the FDCA and recipients	Other	--	7/9/2013	7/9/2013	CDER	Completed	4/5/2013	N	Completed 4/5/2013. The process for issuing non-compliance letters and responses has been implemented. Samples of these letters have been posted: http://inside.fda.gov:9003/CDER/OfficeofNewDrugs/ImmediateOffice/PediatricandMaternalHealthStaff/ucm027829.htm	pdit@fda.hhs.gov

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116	V	505	(b)	NO		Not later than 1 year after enactment, FDA shall issue guidance to implement requirements relating to the submission of plans to study drugs in children	Draft Guidance	7/9/2013	7/9/2013	7/9/2013	CDER	Completed	7/15/2013	Y	FDA is announcing the availability of a draft guidance for industry entitled 'Pediatric Study Plans: Content of and Process for Submitting Initial Pediatric Study Plans and Amended Pediatric Study Plans.' The purpose of this draft guidance is to assist sponsors in the submission of an initial PSP and any amendments to the PSP. The FR Notice published on 7/15/2013 and can be found by following this link: http://www.gpo.gov/fdsys/pkg/FR-2013-07-15/pdf/2013-16828.pdf	pdd@fda.hhs.gov
117	V	505	(a)(1)	NO		Not later than 1 year after enactment, FDA shall promulgate proposed regulations to implement requirements relating to the submission of plans to study drugs in children	Proposed Rule	7/9/2013	12/31/2013	10/30/2014	CDER	In process, on track to meet due date	-	Y		pdd@fda.hhs.gov
118	V	505	(k)(1)	NO		At least 180 days before submission of the report to Congress, FDA shall consult with stakeholders to obtain recommendations including suggestions for modifications that would improve pediatric drug research and labeling	FR Notice	-	1/3/2015		OPT	Scheduled to begin later	-	Y		Debbie Avant debbie.avant@fda.hhs.gov
119	V	505		NO		Not later than 4 years after enactment, FDA shall submit a report to Congress discussing the implementation of the Best Pharmaceuticals for Children Act and the Pediatric Research Equity Act which generally provide for the improved study of drugs in children. The report shall include assessments of the timeliness and effectiveness of pediatric study planning efforts to increase studies in newborns, and information on drugs for pediatric cancers. The report must also be made publicly available on FDA's Internet website	Report to Congress	7/9/2016	7/9/2016	7/1/2016	OPT	In process, on track to meet due date	-	Y		Debbie Avant debbie.avant@fda.hhs.gov
120	V	510	(m)	NO		Not later than 18 months after enactment, FDA shall hold at least one public meeting to discuss ways to encourage/accelerate development of new therapies for pediatric rare diseases	Public Meeting	1/9/2014	1/8/2014		OOPD	Completed	1/8/2014	Y	Meeting was held January 6-8, 2014 as a 3 day public workshop on Complex Issues in Rare Disease Drug Development. Links to additional materials are: http://www.fda.gov/DrugsNewsEvents/ucm397620.htm http://www.fda.gov/MedicalDevices/NewsEvents/WorkshopsConferences/ucm397630.htm	http://www.fda.gov/Drugs/NewsEvents/ucm387622.htm
121	V	510	(n)	NO		Not later than 180 days after the public meeting, FDA shall issue a report that includes a strategy/action for encouraging/accelerating development of new therapies for pediatric rare diseases.	Public Report	-	7/7/2014	7/7/2014	OOPD	In process, on track to meet due date	-	Y		Gaurav Rao (MAY CHANGE)

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122	V	511		NO		The Office of Pediatric Therapeutics shall include an individual with expertise in pediatric epidemiology, and an individual with expertise in in a pediatric subpopulation that is less likely to be studied as part of a written request issued under 505A of the FDCA or an assessment under 505B of the FDCA (for 5 years after enactment the latter individual shall be an individual with expertise in neonatology)	Other	–	–		OPT	In process, on track to meet due date	–	N		Debbie Avant debbie.avant@fda.hhs.gov
123	V	511		NO		The Office of Pediatric Therapeutics shall include an individual with expertise in pediatric epidemiology, and an individual with expertise in in a pediatric subpopulation that is less likely to be studied as part of a written request issued under 505A of the FDCA or an assessment under 505B of the FDCA (for 5 years after enactment the latter individual shall be an individual with expertise in neonatology)	Other	–	–		OPT	In process, on track to meet due date	–	N	–	Debbie Avant debbie.avant@fda.hhs.gov
124	VI	601		NO		FDA intends to revise and re-issue the draft guidance entitled, "FDA Decisions for Investigational Device Exemption (IDE) Clinical Investigations." This guidance, when final, will, among other things, provide FDA's interpretation of and policy on section 601 of FDASIA, which states that FDA may not disapprove an IDE because, among other reasons, the investigation may not support a device clearance or approval or a different investigation may be necessary to support clearance or approval	Draft Guidance	-	6/14/2013	6/14/2013	CDRH	Completed	6/14/2013	Y	"Completed 6/14/2013 http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM279107.pdf"	CDRH FDASIA@fda.hhs.gov
125	VI	603	(b)	NO		FDA intends to issue a final appeals guidance, which will include, among other things, information regarding the requirements under section 603 of FDASIA for a request for a supervisory review of a significant decision	Final Guidance	–	5/17/2013	5/17/2013	CDRH	Completed	5/17/2013	Y	Completed 05/17/2013 http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm284651.htm	CDRH-FDASIA@fda.hhs.gov
126	VI	603		NO		FDA intends to issue a Q&A draft appeals guidance to provide proposed interpretation of key provisions of section 603 of FDASIA, including, among others, what constitutes a "significant decision." When finalized, FDA intends to include the questions and answers in the draft guidance as an appendix to the appeals guidance	Draft Guidance	–	5/30/2013	5/30/2013	CDRH	Completed	5/17/2013	Y	Completed 05/17/2013 http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm352246.htm	CDRH-FDASIA@fda.hhs.gov
127	VI	604		NO		FDA shall withdraw the draft guidance entitled "Guidance for Industry and FDA Staff-510(k) Device Modifications: Deciding When to Submit a 510(k) for a Change to an Existing Device (July 27, 2011)	Other	–	7/17/2012	7/17/2012	CDRH	Completed	7/17/2012	N	Completed 7/17/2012	CDRH-FDASIA@fda.hhs.gov
128	VI	604		NO		FDA shall consider the input of interested stakeholders prior to submitting a report to Congress regarding when a 510(k) premarket notification should be submitted for modifications or changes to a legally marketed device	FR Notice	–	5/8/2013	5/8/2013	CDRH	Completed	5/3/2013	N	Completed 5/3/13 http://www.gpo.gov/fdsys/pkg/FR-2013-05-03/html/2013-10888.htm?source=govdelivery	
129	VI	604		NO		FDA shall consider the input of interested stakeholders prior to submitting a report to Congress regarding when a 510(k) premarket notification should be submitted for modifications or changes to a legally marketed device	Public Meeting	–	6/13/2013	6/13/2013	CDRH	Completed	6/13/2013	N		CDRH-FDASIA@fda.hhs.gov

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130	VI	604		NO		FDA shall submit a report to Congress regarding when a 510(k) premarket notification should be submitted for modifications or changes to a legally marketed device.	Report to Congress	1/5/2014	1/5/2014	1/5/2014	CDRH	Completed	2/25/2014	Y	Completed 2/25/2014 http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDRH/CDRHReports/ucm259873.htm	CDRH-FDASIA@fda.hhs.gov
131	VI	605		NO		FDA intends to improve the Medical Device Recalls database and provide links to the recall database from FDA's 510(k) and PMA databases in order to increase access to safety information on marketed medical devices, as part of the implementation of section 605 of FDASIA, which, among other things, requires FDA to establish a program to routinely and systematically assess information relating to device recalls and to use such information to proactively identify strategies for mitigating health risks presented by defective or unsafe devices.	Other	-	12/13/2013	12/13/2013	CDRH	Completed	12/13/2013	N		CDRH-FDASIA@fda.hhs.gov
132	VI	607		NO		FDA intends to issue a regulation to, among other things, implement the new de novo pathway in section 607 of FDASIA, which does not require a sponsor to first submit a 510(k) before requesting de novo classification.	Proposed Rule	-	5/30/2014	5/30/2014	CDRH	Undergoing FDA Clearance	-	N		CDRH-FDASIA@fda.hhs.gov
133	VI	607		NO		FDA intends to issue a regulation to, among other things, implement the new de novo pathway in section 607 of FDASIA, which does not require a sponsor to first submit a 510(k) before requesting de novo classification.	Final Rule	-	11/30/2015	11/30/2015	CDRH	Scheduled to begin later	-	N		
134	VI	607		NO		In lieu of submitting a report under section 510(k) and subsequent a [de novo] request for classification under clause (a) for a device, if a person determines there is no legally marketed device upon which to base a determination of substantial equivalence ... a person may submit a [de novo] request under this clause for the FDA to classify the device.	Other	-	-		CDRH	Completed	-	Y	FDA is using its authority under this new provision to review "direct" de novo petitions from sponsors (i.e. de novo petitions for devices for which the sponsor did not first submit a 510(k) and receive an NSE decision from FDA)	CDRH-FDASIA@fda.hhs.gov
135	VI	608	(a)(1)	NO		FDA intends to issue a regulation to implement section 608 of FDASIA, which, among other things, amended the procedures for requiring premarket approval for preamendments class III devices under section 515(b) of the FD&C Act and for reclassifying devices under section 513(e) of the FD&C Act to an administrative order process.	Proposed Rule	-	2/28/2014	2/28/2014	CDRH	Undergoing FDA Clearance	-	N		CDRH-FDASIA@fda.hhs.gov
136	VI	608	(a)(1)	NO		Section 608 of FDASIA changed the process for reclassifying devices and requiring premarket approval for preamendment devices from rulemaking to an administrative order process, which includes publication of a proposed order in the Federal Register, consideration of comments, and panel meeting before issuing a final order.	Final Rule	-	8/28/2015	8/28/2015	CDRH	Scheduled to begin later	-	N		
137	VI	608	(a)(1)	NO			Other	-	-		CDRH	Completed	-	Y	FDA is using its authority under this new provision to reclassify devices and call for PMAs by administrative order	CDRH-FDASIA@fda.hhs.gov

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138	VI	608	(c)	NO		FDA shall annually post on its website the number and type of class I and II devices reclassified as class II or III, the number and type of class II and class III devices reclassified as class I or class II, and, the number and types of devices reclassified in the previous calendar year under section 515 of the FD&C Act	[illegible]	–	12/31/2013	12/31/2013	CDRH	Completed	12/17/2013	N		CDRH-FDASIA@fda.hhs.gov
139	VI	611		NO		FDA shall establish and publish in the Federal Register criteria to reaccredit or deny reaccreditation of third-party reviewers (called "Accredited Persons"). Any reaccreditation must specify the particular activities and the devices, for which such persons are accredited to review.	FR Notice	11-9-2012	2/15/2013	2/15/2013	CDRH	Completed	2/15/2013	Y	Action Completed Feb 15, 2013 Link to FR Notice announcing availability of draft guidance http://www.gpo.gov/fdsys/pkg/FR-2013-02-15/html/2013-03538.htm Link to draft guidance http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm339695.htm	CDRH-FDASIA@fda.hhs.gov
140	VI	613		NO		FDA intends to issue guidance that includes an interpretation of section 613 of FDASIA, which, among other things, expands the types of devices approved under a humanitarian device exemption that can be sold for profit. Such devices now include devices intended for treatment or diagnosis of a disease/condition that does not occur in pediatric patients or that occurs in pediatric patients in such numbers that the development of the device for such patients is "impossible, highly impracticable, or unsafe." This guidance, when final, will supersede the guidance entitled "Humanitarian Device Exemption (HDE) Regulation: Questions and Answers," issued July 8, 2010	Draft Guidance	–	3/31/2014	3/31/2014	CDRH	Completed	3/18/2014	Y	Completed 03/18/2014 http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm389154.htm	CDRH-FDASIA@fda.hhs.gov
141	VI	613		NO		FDA intends to issue guidance that includes an interpretation of section 613 of FDASIA, which, among other things, expands the types of devices approved under a humanitarian device exemption that can be sold for profit. Such devices now include devices intended for treatment or diagnosis of a disease/condition that does not occur in pediatric patients or that occurs in pediatric patients in such numbers that the development of the device for such patients is "impossible, highly impracticable, or unsafe." This guidance, when final, will supersede the guidance entitled "Humanitarian Device Exemption (HDE) Regulation: Questions and Answers," issued July 8, 2010	Final Guidance	–	9/30/2015	9/30/2015	CDRH	Scheduled to begin later	–	N	http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm389154.htm	
142	VI	614		NO		FDA must issue final Unique Device Identifier (UDI) regulations not later than 6 months after the close of the comment period for the proposed rule. FDA shall implement these final UDI regulations for devices that are implantable, life-saving, and life-sustaining, not later than 2 years after regulations are finalized	Final Rule	6/19/2013	6/15/2013	9/24/2013	CDRH	Completed	9/24/2013	Y	Completed 9/24/2013 https://www.federalregister.gov/articles/2013/09/24/2013-23059/unique-device-identification-system	CDRH-FDASIA@fda.hhs.gov

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Item #	Title	Section *	Sub-Section	UFA Goals Letter	Goals Letter Citation	Deliverable Description	Deliverable Type	Statutory Deadline *	Targeted Completion Date **	FDA Completion Due Date **	Responsible Organization	Status ***	Date Completed	Publicly Tracked? (FDASIA-TRACK)	FDASIA TRACK Notes (Will be posted on public FDA TRACK Website)	Public Website Contact
143	VI	614		NO		FDA must issue proposed Unique Device Identifier (UDI) regulations by December 31, 2012.	Proposed Rule	12/31/2012	7/10/2012	7/13/2011	CDRH	Completed	7/10/2012	Y	Action Completed 7/10/2012 UDI Proposed Rule 7/10/12 https://www.federalregister.gov/articles/2012/07/10/2012-16931/unique-device-identification-system UDI Amendments to Proposed Rule 11/09/12 https://www.federalregister.gov/articles/2012/11/19/2012-28015/unique-device-identification-system	CDRH-FDASIA@fda.hhs.gov
144	VI	615		NO		FDA shall amend the procedures to expand the postmarket risk identification and analysis system (Sentinel) to include and apply to devices, and engage stakeholders in development of such system.	Public Meeting	-	9/13/2012	9/13/2012	CDRH	Completed	9/13/2012	N	Completed 9/13/2012	CDRH-FDASIA@fda.hhs.gov
145	VI	617		NO		Not later than 2 years after the date of enactment, FDA shall issue final guidance on replication of custom devices used to treat rare conditions such that no other device is domestically available to treat, where conducting a clinical investigation on such device would be impractical, and production of such devices is limited to no more than 5 units per year of the device type.	Draft Guidance	-	1/31/2014	1/31/2014	CDRH	Completed	1/14/2014	Y	Published January 14, 2014. Link to Notice of Availability for draft guidance http://www.gpo.gov/fdsys/pkg/FR-2014-01-14/html/2014-00525.htm	CDRH-FDASIA@fda.hhs.gov
146	VI	617		NO		Not later than 2 years after the date of enactment, FDA shall issue final guidance on replication of custom devices used to treat rare conditions such that no other device is domestically available to treat, where conducting a clinical investigation on such device would be impractical, and production of such devices is limited to no more than 5 units per year of the device type.	Final Guidance	7/9/2014	7/9/2014	7/9/2014	CDRH	Undergoing FDA Clearance	-	Y		CDRH-FDASIA@fda.hhs.gov
147	VI	618	(a)	NO		FDA, in consultation with the National Coordinator for Health Information Technology (ONC) and the Federal Communications Commission (FCC), shall post on the FDA, ONC, and FCC websites, a report containing a proposed strategy and recommendations on an appropriate risk-based regulatory framework pertaining to health information technology, including mobile medical applications, that promotes innovation, protects patient safety, and avoids regulatory duplication.	Public Report	1/8/2014	3/31/2014	2/19/2014	CDRH*	Completed	4/3/2014	Y	Completed 4/3/2014 http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDRH/CDRHReports/ucm350588.htm	CDRH-FDASIA@fda.hhs.gov
148	VI	620	(a)	NO		Not later than December 31, 2012, FDA shall issue a proposed rule that requires submitters to FDA of premarket approval applications (PMAs), supplements to PMAs, humanitarian device exemption applications (HDEs), and product development protocols (PDPs) for devices to include, if readily available, information about pediatric subpopulations that suffer from a disease or condition that the device is intended to treat, diagnose, or cure.	Proposed Rule	12/31/2012	2/19/2013	2/19/2013	CDRH	Completed	2/19/2013	Y	Action Completed Feb 19, 2013 Link to FR notice for Proposed Rule http://www.gpo.gov/fdsys/pkg/FR-2013-02-19/html/2013-03647.htm	CDRH-FDASIA@fda.hhs.gov

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149	VI	620	(b)	NO		Not later than December 31, 2013, FDA shall issue a final rule that requires submitters to FDA of premarket approval applications (PMAs), supplements to PMAs, humanitarian device exemption applications (HDEs), and product development protocols (PDPs) for devices to include, if readily available, information about pediatric subpopulations that suffer from a disease or condition that the device is intended to treat, diagnose or cure.	Final Rule	12/31/2013	12/31/2013	12/31/2013	CDRH	Completed	1/10/2014	Y	Published January 10, 2014 https://www.federalregister.gov/articles/2014/01/10/2014-00237/requirement-for-submission-of-information-on-pediatric-subpopulations-that-suffer-from-a-disease-or	CDRH FDASIA@fda.hhs.gov
150	VI	620	(b)	NO		Not later than December 31, 2012, FDA shall issue a proposed rule that requires submitters to FDA of premarket approval applications (PMAs), supplements to PMAs, humanitarian device exemption applications (HDEs), and product development protocols (PDPs) for devices to include, if readily available, information about pediatric subpopulations that suffer from a disease or condition that the device is intended to treat, diagnose, or cure. FDA intends to issue a companion guidance to this rule. Not later than December 31, 2012, FDA shall issue a proposed rule that requires submitters to FDA of premarket approval applications (PMAs), supplements to PMAs, humanitarian device exemption applications (HDEs), and product development protocols (PDPs) for devices to include, if readily available, information about pediatric subpopulations that suffer from a disease or condition that the device is intended to treat, diagnose, or cure. FDA intends to issue a companion guidance to this rule.	Final Guidance	-	3/31/2014	3/31/2014	CDRH	Completed	5/1/2014	Y	Completed May 1, 2014 http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm339162.htm Action Completed Feb 19, 2013 Link to FR notice http://www.gpo.gov/fdsys/pkg/FR-2013-02-19/html/2013-03652.htm Link to draft guidance http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm339182.htm	CDRH-FDASIA@fda.hhs.gov
151	VI	620	(b)	NO			Draft Guidance	-	2/19/2013	2/19/2013	CDRH	Completed	2/19/2013	Y		
152	VII	701		NO		FDA shall specify the unique facility identifier (UFI) system to be used for domestic and foreign drug establishment registrations.	Draft Guidance	-	9/5/2013	9/5/2013	CDER	Completed	9/5/2013	Y	Completed 09/05/2013 http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM367189.pdf	CDERCompliancePublic@fda.hhs.gov
153	VII	701		NO		FDA shall specify the unique facility identifier (UFI) system to be used for domestic and foreign drug establishment registrations.	Final Guidance	-	4/9/2015	1/29/2015	CDER	In process, on track to meet due date		Y		CDERCompliancePublic@fda.hhs.gov
154	VII	701		NO		FDA will issue a rule that will reorganize, consolidate, clarify, and modify current regulations concerning who must register establishments, and will reflect the requirements for registration of domestic and foreign drug establishments in Sections 701 and 702.	Final Rule	-	4/30/2015	2/27/2015	CDER	In process, on track to meet due date	-	N		CDERCompliancePublic@fda.hhs.gov
155	VII	702		NO		FDA will issue a rule that will reorganize, consolidate, clarify, and modify current regulations concerning who must register establishments, and will reflect the requirements for registration of domestic and foreign drug establishments in Sections 701 and 702.	Final Rule	-	4/30/2015	2/27/2015	CDER	In process, on track to meet due date	-	N		CDERCompliancePublic@fda.hhs.gov

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156	VII	702		NO		FDA will issue a rule that will reorganize, consolidate, clarify, and modify current regulations concerning who must register establishments and will reflect the requirements for registration of domestic and foreign drug establishments in Sections 701 and 702	Draft Guidance	-	9/5/2013	9/5/2013	CDER	Completed	9/5/2013	Y	http://www.fda.gov/downloads/DrugsGuidanceComplianceRegulatoryInformation/Guidances/UCM387199.pdf	CDERCompliancePolicy@fda.hhs.gov
157	VII	702		NO		FDA shall issue a rule that will reorganize, consolidate, clarify, and modify current regulations concerning who must register establishments and will reflect the requirements for registration of domestic and foreign drug establishments in Sections 701 and 702	Final Guidance	-	4/9/2015	11/25/2015	CDER	In process on track to meet due date	-	Y	-	CDERCompliancePolicy@fda.hhs.gov
158	VII	703		NO		Drug listings shall identify the establishments used in production of excipients of the listed drug, including contact information and UFI	Other	-	-	-	CDER	Scheduled to begin later	-	N	-	CDERCompliancePolicy@fda.hhs.gov
159	VII	704		NO		FDA shall maintain an electronic database after specifying a UFI system, and ensure the accuracy and coordination of relevant FDA databases in order to identify and inform risk-based inspections under section 510 of the FD&C Act Starting in 2014, the FDA will publish by February 1 of each year a website report on the number of establishments registered with FDA and inspected by FDA and the percentage of the FDA budget used to conduct these inspections	Database/IT System	-	6/30/2016	6/30/2016	CDER	In process, on track to meet due date	-	N	-	CDERCompliancePolicy@fda.hhs.gov
160	VII	705	a	NO		-	Public Report	1/4/2014	1/31/2014	12/31/2013	CDER	Completed	1/31/2014	Y	Completed 1/31/2014 http://www.fda.gov/downloads/RegulatoryInformation/Legislation/FederalFoodDrugandCosmeticActFDCAct/SignificantAmendmentstotheFDCAct/FDASIA/UCM394063.pdf	CDERCompliancePolicy@fda.hhs.gov
161	VII	705	4(1)(b)	NO		FDA will issue interim policy and procedures for requesting records in the event of a public health incident related to human or animal drugs, including [illegible] [illegible] year after the date of enactment. FDA shall issue guidance that defines the circumstances that would constitute delaying, denying, or limiting inspection or refusing to permit entry or inspection	SOP - New Template	-	7/15/2014	7/15/2014	ORA	In process, on track to meet due date	-	N	-	FDASIAImplementation@ORA@fda.hhs.gov
162	VII	707	(a)	NO		FDA shall issue guidance that defines the circumstances that would constitute delaying, denying, or limiting inspection or refusing to permit entry or inspection	Draft Guidance	7/9/2013	7/15/2013	7/15/2013	ORA	Completed	-	Y	Completed 7/15/2013 https://www.federalregister.gov/articles/2013/07/15/2013-16941/draft-guidance-for-circumstances-that-constitute-delaying-denying-limiting-or-refusing-a	FDASIAImplementation@ORA@fda.hhs.gov
163	VII	707	(d)	NO		Not later than 2 years after the date of enactment, FDA shall issue regulations providing for notice and an opportunity to appear and introduce testimony prior to administrative destruction of a refused admission drug valued under $2,500 Not later than 2 years after the date of enactment, FDA shall issue regulations providing for notice and an opportunity to appear and introduce testimony prior to administrative destruction of a refused admission drug valued at $2,500 or less	Final Guidance		12/22/2014	9/11/2014	ORA	In process, and on track to meet due date	-	Y	-	FDASIAImplementation@ORA@fda.hhs.gov
164	VII	708	(b), (c)	NO			Proposed Rule	-	4/16/2014	10/24/2013	ORA	Completed	5/8/2014	Y	Completed 5/8/2014 https://federalregister.gov/a/2014-10304	FDASIAImplementation@ORA@fda.hhs.gov
165	VII	708	(b), (c)	NO			Final Rule	7/9/2014	9/14/2015	5/7/2015	ORA	In process on track to meet due date	-	Y	-	FDASIAImplementation@ORA@fda.hhs.gov

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166	VII	709	(b)(1)	NO	–	Not later than 2 years after the date of enactment and after consulting with stakeholders including manufacturers of drugs, FDA shall promulgate regulations to implement administrative detention authority with respect to drugs	Final Rule	7/9/2014	7/9/2014	3/21/2014	ORA	In process on track to meet due date	–	Y		FDASIAImplementationORA@fda.hhs.gov
167	VII	709	(b)(2)	NO		Before issuing regulations to implement administrative detention authority with respect to drugs, FDA shall consult with stakeholders, including drug manufacturers	FR Notice	–	4/9/2013	4/9/2013	ORA	Completed	4/28/2013	Y	Completed 4/28/2013 https://www.federalregister.gov/articles/text/raw_text/201/308/120.txt	FDASIAImplementationORA@fda.hhs.gov
168	VII	709	(b)(2)	NO		Not later than 2 years after date of enactment and after consulting with stakeholders including drug manufacturers, FDA shall issue regulations to implement administrative detention authority with respect to drugs	Proposed Rule	–	7/15/2013	7/15/2013	ORA	Completed	–	Y	Completed 7/15/2013 https://www.federalregister.gov/articles/2013/07/15/2013-16843/administrative-detention-of-drugs-intended-for-human-or-animal-use	FDASIAImplementationORA@fda.hhs.gov
169	VII	711		NO		FDA may revise regulations to implement Section 711 and other Sections of Title VII	Proposed Rule	–	1/4/2016	9/21/2015	CDER	In process, on track to meet due date	–	Y		CDERCompliancePublic@fda.hhs.gov
170	VII	711		NO		FDA may revise regulations to implement Section 711 and other Sections of Title VII	Final Rule	–	4/7/2017	10/3/2016	CDER	In process on track to meet due date	–	Y		CDERCompliancePublic@fda.hhs.gov
171	VII	713		NO		Not later than 18 months after the date of enactment, FDA shall adopt final regulations which may require importers to submit certain electronic information as a condition of import	Final Rule	7/9/2014	7/10/2017	9/2/2016	CDER	In process on track to meet due date	–	Y		CDERCompliancePublic@fda.hhs.gov
172	VII	713		NO		Not later than 18 months after the date of enactment, FDA shall adopt final regulations which may require importers to submit certain electronic information as a condition of import.	Proposed Rule	–	9/25/2015	5/20/2015	CDER	In process, on track to meet due date	–	Y		CDERCompliancePublic@fda.hhs.gov
173	VII	714	(b)	NO		Not later than 18 months after date of enactment, FDA, in consultation with the Secretary of Homeland Security, acting through Customs and Border Protection, shall issue regulation to establish good importer practices for drugs	Proposed Rule	–	4/29/2015	12/25/2014	OP	In process and on track to meet due date	–	Y		Brian Pendleton brian.pendleton@fda.hhs.gov
174	VII	714	(b)	NO		Not later than 36 months after date of enactment, FDA, in consultation with the Secretary of Homeland Security acting through Customs and Border Protection, shall issue regulation to establish good importer practices for drugs	Final Rule	7/9/2015	1/31/2017	9/8/2016	OP	In process on track to meet due date	–	Y		Brian Pendleton brian.pendleton@fda.hhs.gov
175	VII	714	(a), (b)	NO		Not later than 36 months after the date of enactment, FDA, in consultation with the Secretary of Homeland Security acting through Customs and Border Protection, shall issue regulations to require registration of commercial importers of drugs	Final Rule	7/9/2015	1/31/2017	9/8/2016	OP	In process and on track to meet due date	–	Y		Brian Pendleton brian.pendleton@fda.hhs.gov

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176	VII	714	(c), (d)	NO		Not later than 36 months after the date of enactment FDA, in consultation with the Secretary of Homeland Security acting through Customs and Border Protection, shall issue regulations to require registration of commercial importers of drugs	Proposed Rule	–	4/29/2015	12/26/2014	OP	Inprocess and ontrack to meet due date	–	Y		Brian Pendleson brian.pendleton@fda.hhs.gov
177	VIII	801	(a)	NO		Not later than 2 years after the date of enactment, FDA shall adopt final regulations, following specified procedures, to implement this section, including establishing a list of qualifying pathogens	Final Rule	7/9/2014	7/7/2014	12/15/2013	CDER	In process on track to meet due date	–	Y	–	druginfo@fda.hhs.gov
178	VIII	801	(a)	NO		Not later than 2 years after the date of enactment, FDA shall adopt final regulations, following specified procedures, to implement this section, including establishing a list of qualifying pathogens	Proposed Rule	–	5/30/2013	6/5/2013	CDER	Completed	6/5/2013	Y	FR Notice released 6/5/2013. Public comment period ends on 8/12/2013. FDA has published a proposed rule that establishes a proposed list of "qualifying pathogens" that have the potential to pose a serious threat to public health and describes the methodology for creating and maintaining the list. Establishing this list is related to FDA's efforts to encourage the development of new antibacterial and antifungal drugs for the treatment of serious or life threatening infections. http://www.regulations.gov/#!documentDetail;D=FDA-2012-N-1037-0013 6/5/2013: Proposed Rule for 801 contains the proposed list http://www.regulations.gov/#!documentDetail;D=FDA-2012-N-1037-0013 Open for public comment until 8/12/2013	druginfo@fda.hhs.gov
[illegible]	VIII	801	(c)	NO		At least every 5 years FDA shall review, modify and publish the list of qualifying pathogens and issue a regulation revising the list as needed. FDA shall consult with CDC and others when establishing the list and make the methodology for developing the list publicly available	List	7/2/2017	7/2/2014	1/15/2014	CDER	Substantially complete, on track to meet due date	–	Y	Consulted with CDC and NIH via public meeting (Part 15 Hearing) http://www.fda.gov/Drugs/NewsEvents/ucm319610.htm	druginfo@fda.hhs.gov

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180	VIII	804	a(1)	NO		FDA shall review and, if needed, revise no fewer than 3 guidance documents per year regarding the conduct of clinical trials for antibacterial and antifungal drugs	Other	7/9/2013	7/9/2013	10/12/2012	CDER	Completed	10/12/2012	Y	1. Chronic Bronchitis in Patients with Chronic Obstructive Pulmonary Disease: Final published 09/26/12 (conversion of draft guidance to final) http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm321330.htm 2. Acute Bacterial Otitis Media: Final published 10/01/12 (conversion of draft guidance to final) http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm322763.htm 3. Acute Bacterial Sinusitis: Final published 10/05/12 (conversion of draft guidance to final) http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm322630.htm	druginfo@fda.hhs.gov
181	VIII	805		NO		FDA shall submit a report to Congress on the designation, review and approval of qualified infectious disease products and recommendations regarding qualifying pathogens and any additional programs or incentives that may be needed to promote the development of antibacterial drugs	Report to Congress	7/7/2017	7/7/2017	3/1/2017	HHS/CDER	Scheduled to begin later	-	Y		druginfo@fda.hhs.gov
182	VIII	806	(a)	NO		Not later than June 30, 2013, FDA shall publish draft guidance that addresses how data may be used for the efficient and streamlined development of antibacterial drugs to treat serious or life-threatening bacterial infections, including approaches for developing limited-spectrum antibacterials	Draft Guidance	6/28/2013	5/28/2013	5/28/2013	CDER	Completed	7/1/2013	Y	FDA Webinar presented on new Draft Guidance for industry on 9/27/2013 Completed 7/1/2013 Draft Guidance published http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM359184.pdf	http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM359184.pdf
183	VIII	806	(b)	NO		Not later than December 31, 2014, FDA shall publish final guidance, after notice and opportunity for public comment, that addresses how data may be used for the efficient and streamlined development of antibacterial drugs to treat serious or life-threatening bacterial infections	Final Guidance	12/31/2014	12/18/2014	10/30/2014	CDER	In process - on track to meet due date	-	Y		druginfo@fda.hhs.gov
184	X	901	(b)	NO		Awareness Efforts: FDA shall (1) develop and disseminate to certain groups listed in the statute a description of provisions on accelerated approval and fast track products, and (2) establish a program to encourage the development of surrogate and clinical endpoints and other scientific methods and tools to assist in determining whether evidence is reasonably likely to predict clinical benefit	Other	-	6/30/2015	6/30/2015	CDER	Scheduled to begin later	-	N		druginfo@fda.hhs.gov

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155	IX	901	(c)	NO		Not later than 1 year after the date of enactment, FDA shall issue draft guidance on the clarified standard for accelerated approval and fast track processes including issues for drugs for a rare disease or condition	Draft Guidance	7/9/2013	7/9/2013	6/17/2013	CDER	Completed	6/25/2013	Y	Completed 6/25/2013 Draft Guidance for Industry: Expedited Programs for Serious Conditions--Drugs and Biologics http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM358301.pdf	druginfo@fda.hhs.gov
156	IX	901	(c)	NO		Not later than 1 year after the issuance of draft guidance, FDA shall issue final guidance on the clarified standard for accelerated approval and fast track processes, including issues for a rare disease or condition	Final Guidance	7/9/2014	7/5/2014	5/15/2014	CDER	In process on track to meet due date	–	Y		druginfo@fda.hhs.gov
161	IX	902	(c)	NO		Not later than 18 months after the date of enactment, FDA shall issue draft guidance implementing the requirements on breakthrough therapies to treat a serious or life-threatening condition where early evidence shows the drug may offer substantial improvement over existing treatments	Draft Guidance	1/9/2014	1/9/2014	6/26/2013	CDER	Completed	6/25/2013	Y	Completed 6/26/13 Draft Guidance for Industry: Expedited Programs for Serious Conditions--Drugs and Biologics http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM358301.pdf Federal Register Notice https://www.federalregister.gov/articles/2013/06/26/2013-15200/draft-guidance-for-industry-on-expedited-programs-for-serious-conditions-drugs-and-biologics	druginfo@fda.hhs.gov
162	IX	902	(c)	NO		Not later than 1 year after the close of the comment period for the draft guidance, FDA shall issue draft final guidance on implementing the requirements with respect to breakthrough therapies to treat a serious or life-threatening condition where early evidence shows the drug may offer substantial improvement over existing treatments	Final Guidance	7/9/2014	7/9/2014	6/9/2014	CDER	In process on track to meet due date	–	Y		druginfo@fda.hhs.gov
189	IX	903	(a)(b)	NO		(1) FDA shall ensure that opportunities exist for consultations with stakeholders, when appropriate and consistent with PDUFA on the topics described in section 903(b) related to rare diseases. (2) FDA shall develop and maintain a list of external experts for consultation on issues related to the review of new drugs and biological products for rare diseases and drugs and biological products that are genetically targeted	List	-	-		CDER	Completed	2/28/2013	N	In the Center for Drug Evaluation and Research (CDER), the Division of Advisory Committee and Consultant Management (DACCM) maintains an extensive list of special government employees (SGEs) for advisory committees (ACs) and other consultative needs. Currently DACCM has a listing of approximately 1,200 SGEs categorized by therapeutic area expertise, many of whom are on the roster for a specific AC. Depending on the drug and disease under discussion, ACs may be supplemented with temporary members to provide additional expertise on the topic. Many diseases have multi-system effects so it is useful for FDA to have access to a diverse list of experts from a variety of fields available for consultation	druginfo@fda.hhs.gov

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Item #	Title	Section *	Sub-Section	UFA Goals Letter	Goals Letter Citation	Deliverable Description	Deliverable Type	Statutory Deadline *	Targeted Completion Date **	FDA Completion Due Date **	Responsible Organization	Status ***	Date Completed	Publicly Tracked?(FDASIA-TRACK)	FDASIA TRACK Notes (Will be posted on public FDA-TRACK Website)	Public Website Contact
190	IX	904	(b)	NO		GAO study regarding the extent to which pharmacies are utilizing best practices and the extent to which barriers to accessible information on prescription drug container labels for blind and visually impaired individuals continue; requires the study to cap 1-18 months after completion of the assessment of best practices and to be submitted to Congress no later than September 30, 2015	GAO Report	9/30/2015	9/30/2015	9/30/2015	GAO/OPP	Scheduled to begin later	-	Y		Claudia Grillo Claudia.grillo@fda.hhs.gov
191	IX	904		NO		The Architectural and Transportation Barriers Compliance Board to convene a stakeholder working group to develop best practices on access to information on a prescription drug container labels for individuals who are blind or visually impaired within 1 year of enactment. National Council on Disability shall conduct educational campaign about best practices	Public Report	7/9/2013	7/9/2013		CDER/Architectural and Transportation Barriers Compliance Board	Completed	7/10/2013	N	Completed 7/10/2013 link "www.access-board.gov/guidelines-and-standards/health-care/about-this-project-on-prescription-container-labels/working-group-recommendations	CDER EXECSEC for CDER
192	IX	907	a1	NO		Not later than 1 year after enactment, FDA will issue a report that describes the participation of demographic subgroups (sex, age, race, and ethnicity) in clinical studies submitted to FDA in marketing applications. The report will also describe the inclusion of safety and effectiveness data for demographic subgroups in marketing applications submitted to FDA. The report will be posted on FDA's website and provided to Congress No later than 1 year after preparing the report to Congress, FDA shall publish an action plan on the FDA website with recommendations on improving the completeness and quality of data analyses on demographic subgroups, including such data in labeling, and making such data available to patients and providers	Public Report	7/9/2013	7/9/2013	7/9/2013	OWH	Completed	8/23/2013	Y	Completed 8/20/2013 link "www.fda.gov/downloads/RegulatoryInformation/Legislation/FederalFoodDrugandCosmeticActFDCAct/SignificantAmendmentstotheFDCAct/FDASIA/UCM365541.pdf	Pamela.Scott@fda.hhs.gov
193	IX	907	(b)	NO		FDA shall establish a user fee program under which a sponsor of a human drug application that is the subject of a priority review voucher shall pay a fee, determined based on the differences between the average cost incurred by FDA in the review of a human drug application subject to priority review in the previous year, and the average cost incurred by FDA in the review of a human drug application not subject to priority review in the previous year	Plan	8/20/2014	8/20/2014	8/20/2014	OMH	In process on track to meet the date	-	Y		Jeanie.Bull@fda.hhs.gov
194	IX	908		NO		GAO shall study the effectiveness of awarding rare pediatric disease products priority review vouchers on the development of human drug products that treat or prevent such diseases.	FR Notice	-	-	-	OPL	Scheduled to begin later	-	N		Clark.Nardinelli@fda.hhs.gov
195	IX	908		NO			GAO Report	-	-	-	GAO/OPP	Scheduled to begin later	-	N		Claudia Grillo Claudia.grillo@fda.hhs.gov
196	IX	908		NO		When after the last day of the 1-year period that begins on the date that FDA awards the third rare pediatric disease priority voucher, a sponsor of an application uses such a voucher, FDA shall submit a document to Congress notifying them of the use of such voucher and identifying the drug for which it was used.	Report to Congress	-	-	-	OOPD	Scheduled to begin later	-	N		drugpolicy@fda.hhs.gov
197	IX	908		NO		FDA shall publish in the Federal Register notice of issuance of voucher and approval of products using a priority review voucher	FR Notice	-	-	-	OOPD	Scheduled to begin later	-	N		drugpolicy@fda.hhs.gov

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FOOD AND DRUG SAFETY AND INNOVATION ACT (FDASIA) INTERNAL TRACKING SHEET

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Item #	Title	Section *	Sub-Section	UFA Goals Letter	Goals Letter Citation	Deliverable Description	Deliverable Type	Statutory Deadline *	Targeted Completion Date **	FDA Completion Due Date **	Responsible Organization	Status ***	Date Completed	Publicly Tracked? (FDASIA-TRACK)	FDASIA TRACK Notes (Will be posted on public FDASIA-TRACK Website)	Public Website Content
198	X	1001	(a)	NO		Not later than 18 months after the date of enactment FDA shall adopt final regulations implementing provisions regarding drug shortages, including defining certain terms	Proposed Rule	-	7/9/2013	10/23/2013	CDER	Completed	10/31/2013	Y	FDA has the proposed rule "Permanent Discontinuance or Interruption in Manufacturing of Certain Drug or Biological Products" issued. If finalized, the rule will expand the requirement for drug and biologic manufacturers to notify FDA early about issues that could lead to a potential shortage. The FR notice Published on 10/31/2013 https://federalregister.gov/a/2013-25956	http://www.fda.gov/Drugs/DrugSafety/DrugShortages/default.htm
199	X	1001	(a)	NO		Not later than 18 months after the date of enactment FDA shall adopt final regulations implementing provisions regarding drug shortages, including defining certain terms	Final Rule	1/9/2014	1/9/2014		CDER	In process, delayed and may not meet due date	-	Y	FDA issued a proposed rule on 10/31/2013 and has requested public comments	https://www.federalregister.gov/articles/2013/11/04/2013-25956/permanent-discontinuance-or-interruption-in-manufacturing-of-certain-drug-or-biological-products
200	X	1001	(c)	NO		To the maximum extent practicable, FDA shall distribute information on the discontinuation or interruption of the manufacture of drugs (about which FDA is notified) to appropriate organizations including physicians, health care providers, patient organizations	Website	7/9/2012	7/9/2012	7/9/2012	CDER	Completed	7/9/2012	N		http://www.fda.gov/Drugs/DrugSafety/DrugShortages/default.htm
201	X	1001	(e)	NO		FDA shall determine whether a notification of shortage pertains to a controlled substance subject to a production quota under section 306 of the CSA and, if necessary, notify the Attorney General of a discontinuance of a controlled substance and request DOJ to increase the quota	Other	7/9/2012	7/9/2012	7/9/2012	CDER	Completed	-	N		http://www.fda.gov/Drugs/DrugSafety/DrugShortages/default.htm
202	X	1002		NO		FDA shall submit an annual report to Congress providing information on drug shortages, including information on the agency's efforts to prevent or mitigate shortages	Report to Congress	12/31/2013	12/31/2013	12/1/2013	CDER	Completed	2/6/2014	Y	Completed 2/6/2014 Drug Shortages Report to Congress - http://www.fda.gov/Drugs/DrugSafety/DrugShortages/ucm384891.htm	http://www.fda.gov/Drugs/DrugSafety/DrugShortages/default.htm
203	X	1003	(d)	NO		[illegible] enforcement action or issuance of a warning letter that the Secretary determines could reasonably be anticipated to lead to a meaningful disruption in the supply in the U.S. of a drug under 506C(a), there is a communication with the appropriate office of the FDA with expertise regarding drug shortages regarding whether the action or letter could cause, or exacerbate, a shortage of the drug; if so, the Secretary shall evaluate the risks associated with the impact of such shortage upon patients and those risks associated with the violation involved before taking such action or issuing such letter, unless there is imminent risk of serious adverse health consequences or death to humans"	SOP - New Template	-	-		CDER	Scheduled to begin later	-	N		CDERCompliancePub s@fda.hhs.gov

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204	X	1003	a	NO		FDA shall identify or establish a mechanism by which health care providers and other third-party organizations may report to FDA evidence of a drug shortage	Other	–	12/18/2013	12/18/2013	CDER	Completed	12/11/2013	Y	Completed 01/11/2013 http://www.fda.gov/Drugs/DrugSafety/DrugShortages/ucm142398.htm	http://www.fda.gov/Drugs/DrugSafety/DrugShortages/default.htm
205	X	1003		NO		FDA shall establish a task force to develop and implement a strategic plan for enhancing the Secretary's response to preventing and mitigating drug shortages	Strategic Plan	7/9/2013	7/9/2013	10/31/2013	CDER	Completed	10/31/2013	Y	The Agency has issued a long-term strategic plan that focuses on preventing many of the underlying causes of most drug shortages. The plan outlines the Agency's strategy for improving its response to early notifications of a potential shortage, as well as long-term tactics to address the underlying causes of shortages. Plan published and can be accessed through this link: http://www.fda.gov/downloads/Drugs/DrugSafety/DrugShortages/UCM372566.pdf	http://www.fda.gov/Drugs/DrugSafety/DrugShortages/default.htm
206	X	1003		NO		Not later than one year after the date of enactment FDA shall publish the drug shortage strategic plan and submit the report to Congress	Public Report	7/9/2013	7/5/2013	7/9/2013	CDER	Completed	10/31/2013	N	First, the agency has issued a long-term strategic plan that focuses on preventing many of the underlying causes of most drug shortages. The plan outlines the Agency's strategy for improving its response to early notifications of a potential shortage, as well as long-term tactics to address the underlying causes of shortages	http://www.fda.gov/downloads/Drugs/DrugSafety/DrugShortages/UCM372566.pdf
207	X	1005		NO		Attorney General shall promptly review requests for an adjustment in aggregate quotas made by the manufacturer of a schedule II drug on FDA's drug shortage list. If the AG determines the level requested is not necessary to address a shortage, the AG shall provide a written response detailing the basis for such determination. The Secretary shall make such a written response available to the public on the FDA website	Public Report	–	–		CDER/DOJ	Other	–	N		drugshortages@fda.hhs.gov
208	X	1006		NO		Attorney General shall submit a report to Congress identifying the number of requests it receives to adjust quotas for drugs in shortage, and the number of requests granted and denied, and the reason for each denial. The report must also describe the coordination between DEA and FDA on efforts to prevent or alleviate drug shortages.	Report to Congress	1/9/2013	-		CDER/DOJ	Other	–	N		drugshortages@fda.hhs.gov
209	X	1007		NO		Allows hospitals to repackage certain drugs in shortage into smaller doses for transfer within the same healthcare system without having to register with FDA. This section sunsets if FDA issues guidance on this issue	Final Guidance	–	–		CDER	Scheduled to begin later	–	N		CDERComplianceFublic@fda.hhs.gov
210	X	1008		NO		GAO shall conduct a study to examine the cause of and give recommendations on how to prevent or alleviate drug shortages in the United States. GAO shall report the results of the study to Congress	GAO Report	1/9/2014	2/7/2014	2/7/2014	GAO-OPP	Completed	2/10/2014	N	GAO has completed and published the report: http://www.gao.gov/products/GAO-14-194	drugshortages@fda.hhs.gov

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211	XI-B	1112	(a)	NO	Not later than 18 months after the date of enactment, FDA shall determine whether any changes to FDA drug regulations are necessary for medical gases. FDA will obtain input from medical gas manufacturers and other interested members of the public about whether changes are needed. The agency will submit a report to Congress regarding any changes to the regulations. If FDA determines that any changes to the Federal drug regulations are necessary for medical gases pursuant to Sec. 1112 (a) (1), FDA shall issue revised regulations.	Report to Congress	1/9/2014	1/9/2014	1/9/2014	CDER	In Process, delayed and did not meet the due date		Y	On 11/13/13, announced public meeting to be held on 12/6/2013, on whether any changes to Federal drug regulations are necessary for medical gases: https://federalregister.gov/a/2013-26952 Created a certification program for designated medical gases (1111) Comments on Certification (FDASIA Section 1111): http://www.regulations.gov/#!documentDetail;D=FDA-2012-N-1040-0001 3/22/2013: Opened the docket for the Med Gas Reg Medical Gases--Medical Gases--Comments to Changes in Regulations (FDASIA Section 1112) http://www.regulations.gov/#!documentDetail;D=FDA-2012-D-0501-0003	CDERCompliance@fda.hhs.gov
212	XI-B	1112	(b)	NO		Proposed Rule	7/9/2015	7/9/2015	10/30/2015	CDER	Scheduled to begin later		N		CDERCompliance@fda.hhs.gov drugsfo@fda.hhs.gov
213	XI-C	1121		NO	Not later than 2 years after the date of enactment, FDA shall issue guidance describing FDA policy regarding internet promotion, including social media, of medical products regulated by FDA.	Draft Guidance	7/9/2014	7/9/2014	3.15.2014	CDER/OMP/OPDP	In process, on track to meet due date		Y	drugsfo@fda.hhs.gov	drugsfo@fda.hhs.gov
214	XI-C	1122	(a)	NO	To fight the significant rise in prescription drug abuse, FDA, in coordination with other federal agencies as appropriate, shall review federal initiatives and identify gaps and opportunities regarding the safe use of prescription drugs with potential for abuse and the treatment of prescription drug dependence.	Other	7/9/2013	-	7/9/2013	CDER/OASH	Completed	3/20/2013	N	Completed 03/20/2013	Dwgiale@fda.hhs.gov
215	XI-C	1122	(b)	NO	Not later than one year after the date of enactment, the Secretary of Health and Human Services will post on the HHS Internet website a report on the findings of the review of federal initiatives, gaps, and opportunities regarding the safe use of prescription drugs with potential for abuse and the treatment of prescription drug dependence.	Public Report	7/9/2013	7/9/2013	10/23/2013	CDER/OASH/CDC	Completed	10/23/2013	N	Report was sent to Congress 10/23/2013 CDC is working with OASH to post the report on the web CDER and DER have a copy of the Report. http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM334745.pdf	Dwgiale@fda.hhs.gov drugsfo@fda.hhs.gov
216	XI-C	1122	(c)	NO	Not later than 6 months after the date of enactment, FDA shall promulgate guidance on the development of abuse-deterrent drug products.	Draft Guidance	1/9/2013	1/9/2013	11/20.2012	CDER	Completed	1/9/2013	Y		
217	XI-C	1123		NO	FDA shall (1) work with other regulatory authorities to foster and encourage uniform, scientifically driven clinical trial standards with respect to medical products around the world, (2) enhance consistency to provide consistent parallel advice to manufacturers seeking simultaneous global development of new medical products.	Other	-	-		OPP	Scheduled to begin later	-	N		

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6.4.2014

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218	XI-C	1123		NO		FDA shall accept data from clinical investigations conducted outside the U.S. for drug and device applications if the applicant demonstrates that such data are adequate under applicable standards for approval in United States. FDA shall provide written notice to the sponsor if FDA finds the foreign data to be inadequate and provide a rationale for this finding.	SOP - New Template	-	-		OPP	Scheduled to begin later	-	N		
219	XI-C	1124		NO		Not later than 1 year after the date of enactment, FDA shall develop a strategy and implementation plan for advancing regulatory science for medical products in order to promote the public health and advance innovation in regulatory decision-making. The plan developed must be consistent with the goals established in the user fee negotiations for drugs and biologics (PDUFA), devices (MDUFA), generic drugs (GDUFA), and biosimilars (BSUFA).	Strategic Plan	7/9/2013	7/9/2013	7/9/2013	OPL	Completed	7/9/2013	Y	Completed 7/9/2013 http://www.fda.gov/downloads/RegulatoryInformation/Legislation/FederalFoodDrugandCosmeticActFDCAct/SignificantAmendmentstotheFDCAct/FDASIA/UCM359856.pdf	Dahan Tarver dahan.tarver@fda.hhs.gov
220	XI-C	1124		NO		For fiscal years 2014 through 2018 FDA shall include information on the progress made in advancing regulatory science in the annual performance reports on the implementation of the user fee programs for drugs and biologics (PDUFA), devices (MDUFA), generic drugs (GDUFA), and biosimilars (BSUFA).	Report to Congress	1/31/2015	1/31/2015	1/31/2015	OPL	Scheduled to begin later	-	Y		Dahan Tarver dahan.tarver@fda.hhs.gov
221	XI-C	1125		NO		Not later than 1 year after the date of enactment, FDA shall submit a report to Congress on the measures and a completion date for developing and implementing a comprehensive information technology strategic plan, a comprehensive inventory of FDA's information technology systems, how FDA uses the strategic plan to guide the agency's modernization process, and the extent to which FDA is implementing information technology recommendations of the Government Accountability Office.	Report to Congress	7/9/2013	7/9/2013	8/10/2013	OC (CIM)	Completed	11-4-2013	Y	Completed 11/4/2013	Carolyn Yancey Carolyn.Yancey@fda.hhs.gov
222	XI-C	1125		NO		GAO is required to report on the comprehensive IT plan and the implementation of such plan by the FDA, reporting progress made by the FDA.	GAO Report	12/31/2015	12/31/2015	12/31/2015	GAO/OPP	Scheduled to begin later	-	N		Claudia Grillo Claudia.grillo@fda.hhs.gov
223	XI-C	1126		NO		Requires various ongoing efforts related to regulatory science regarding nanotechnology in FDA-regulated products.	Other	-	8/1/2013	8/1/2013	OCS	Completed	8/1/2013	N	First Report issued 7/13/13: Internal Pharmacist, Federal Agencies and States Face Challenges Combating Rogue Sites http://www.gao.gov/products/GAO-13-560	Jed Costanza jed.costanza@fda.hhs.gov
224	XI-C	1127		NO		GAO report on online pharmacy websites that violate state or federal law.	GAO Report	7/9/2013	7/9/2013	7/9/2013	GAO/OPP	Completed	7/13/2013	N		http://www.gao.gov/products/GAO-13-560
225	XI-C	1128		NO		Not later than one year after the date of enactment, FDA shall submit a report to Congress on the agency's small business assistance activities, including information on all of FDA's small business assistance offices, sponsorship efforts between FDA and the Small Business Administration, outreach efforts to small businesses, and other specified topics.	Report to Congress	7/9/2013	7/9/2013	8/17/2013	OP	Completed	7/9/2013	Y	Completed July 9, 2013 http://www.fda.gov/downloads/RegulatoryInformation/Legislation/FederalFoodDrugandCosmeticActFDCAct/SignificantAmendmentstotheFDCAct/FDASIA/UCM360858.pdf	

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226	XI-C	1131		NO		Not later than one year after enactment, FDA will submit a report to Congress on a strategic management plan for CDER, CBER, and CDRH which will include goals and priorities for improving efficiency, actions that will develop the workforce at all the centers, and the mechanisms that will be used to measure progress in achieving the goals of the plan	Strategic Plan	7/9/2013	7/9/2013	8/14/2013	OPL	Completed	7/9/2012	Y	Completed July 9, 2013 http://www.fda.gov/downloads/RegulatoryInformation/Legislation/FederalFoodDrugandCosmeticActFDCAct/SignificantAmendmentstotheFDCAct/FDASIA/UCM360047.pdf	Patricia Stewart patricia.stewart@fda.hhs.gov
227	XI-C	1132	(b)(c)	NO		Not later than 1 year after the date of enactment, FDA shall issue guidance describing the types of modifications to approved Risk Evaluation and Mitigation Strategies that shall be considered to be minor modifications of such strategies for the purposes of section 505-1(h)(2)(A)	Draft Guidance	7/9/2013	7/9/2013	7/9/2013	CDER	Undergoing FDA Clearance	–	Y		druginfo@fda.hhs.gov
228	XI-C	1136		NO		Beginning at least two years after FDA finalizes a guidance that specifies the electronic format for any submission related to an IND, BLA, or NDA, all such submissions must be made in the format specified in such guidance."	Draft Guidance	–	1/31/2014	1/31/2014	CDER	Completed	2-6-2014	N	Completed 2/6/2014 FDASIA Electronic Submissions Guidance http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM384686.pdf	
229	XI-C	1136		NO		Beginning at least two years after FDA finalizes a guidance that specifies the electronic format for any submission related to an IND, BLA, or NDA, all such submissions must be made in the format specified in such guidance."	Final Guidance	–	9/30/2014	5/30/2014	CDER	In process on track to meet due date		N		
230	XI-C	1136		NO		"Beginning after the issuance of final guidance presubmissions and submissions for devices and any supplements to such presubmissions or submissions, shall include an electronic copy of such presubmissions or submissions."	Final Guidance	–	12/31/2012	12/31/2012	CDRH	Completed	12/31/2012	N	Action Completed Dec 31, 2012 http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM313794.pdf	
231	XI-L	1137		NO		FDA shall develop and implement strategies to solicit patients' views during the medical product development and regulatory processes, including fostering participation of a patient representative who may serve as a special government employee in appropriate agency meetings with medical product sponsors and investigators exploring means to provide for identification of patient representatives who do not have any, or have minimal, financial interests in the medical products industry	Plan	–	–		OSHI	Scheduled to begin later	–	N		
232	XI-C	1138		NO		Not later than one year after the date of enactment, FDA must issue a communication plan to inform and educate health care providers and patients with a particular focus on underrepresented subpopulations, on the benefits and risks of medical products. FDA must seek public comment on the communication plan and post it on the agency's internet website	Plan	7/9/2013	7/9/2013	7/9/2013	OMH, OPA	Completed	7/9/2013	Y	Completed 07/09/2013 http://www.fda.gov/downloads/RegulatoryInformation/Legislation/FederalFoodDrugandCosmeticActFDCAct/SignificantAmendmentstotheFDCAct/FDASIA/UCM359990.pdf Will open docket for comment on the plan	Jonca Bull@fda.hhs.gov

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FOOD AND DRUG SAFETY AND INNOVATION ACT FDASIA - INTERNAL TRACKING SHEET

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Item #	Title	Section *	Sub-Section	UFA Goals Letter	Goals Letter Citation	Deliverable Description	Deliverable Type	Statutory Deadline *	Targeted Completion Date **	FDA Completion Due Date **	Responsible Organization	Status ***	Date Completed	Publicly Tracked? (FDASIA-TRACK)	FDASIA TRACK Notes (to be posted on public FDA TRACK Website) http://www.fda.gov/AdvisoryCommittees/Calendar/ucm332857.htm	Public Website Contact
233	XI-C	1139		NO		Not later than 60 days after the date of enactment of [illegible] FDA must hold a public meeting to ask for advice and recommendations to help make scheduling recommendations to the Drug Enforcement Administration regarding drugs that contain hydrocodone, either combined with other pain medicines (analgesics) or used as a cough medicine (antitussive)	Public Meeting	9/7/2012	10/29/2012		CDER	Completed	1/24/2013	Y	This meeting was rescheduled to January 2013 due to the postponement of the October 29-30, 2012 because of the unanticipated weather conditions caused by Hurricane Sandy	CDER EXECSEC
234	XI-C	1140		NO		GAO study on benefits and efficiencies of electronic patient [illegible] prescription drugs	GAO Report	7/9/2013	7/9/2013	7/9/2013	GAO/OPP	Completed	8/1/2013	N	Final Report issued 8/1/13. GAO released the final report on Electronic Drug Labeling: No Consensus on the [illegible] and [illegible] of its [illegible] Use http://www.gao.gov/products/GAO-13-592	http://www.gao.gov/products/GAO-13-592
235	XI-C	1141		NO		The Secretary may [illegible], as appropriate, may consult with the Attorney General to facilitate, to develop recommendations for interoperability standards to exchange prescription drug monitoring information across state lines by states receiving grants under the Harold Rogers Prescription Drug Monitoring Program (PDMP) and the Controlled Substance Monitoring Program. The section also imposes requirements for information to consider when developing recommendations	Plan	7/9/2013	7/9/2013	10/23/2013	CDER/CDC	Completed	10/23/2013	N	CDC sent report to Congress on 10/23/2013. CDC is working on publishing the 1141 report on the web. OGI and CDER have copies of the report.	[illegible]@fda.hhs.gov
236	XI-C	1141		NO		Not later than one year after the date of enactment FDA must submit a report to Congress on enhancing the interoperability of State prescription drug monitoring programs with other technologies used for detecting and reducing fraud, diversion, and abuse of prescription drugs	Report to Congress	7/9/2013	7/9/2013	10/23/2013	CDER/SAMHSA/ONCDP	Completed	10/23/2013	N	Report has not been posted on any public web page as of 10/23/2013. But CDER has a copy of the final report that has already been sent to the HJ	druginfo@fda.hhs.gov
237	XI-C	1142	(a)(1)	NO	NA	Not later than February 1 of each year, FDA shall submit a report to Congress describing specific information on FDA advisory committees including such things as the number of people nominated to the committees, the number who are nominated and willing to serve, the number of vacancies on committees, and the number of people contacted to serve on a committee who did not because of the [illegible] for their participation to constitute a disqualifying financial interest under federal law	Report to Congress	2/1/2014	2/1/2014	2/1/2014	ACOMS	Completed	2/3/2014	Y	Completed 02/03/2014. http://www.fda.gov/downloads/AdvisoryCommittees/AboutAdvisoryCommittees/UCM395811.pdf	Michael Ortwerth michael.ortwerth@fda.hhs.gov
238	XI-C	1142	(a)(2)	NO	NA	Not later than 30 days after submitting any report under 712(a)(1) of the FDCA to Congress, FDA shall make the report available to the public.	Public Report	3/1/2014	3/1/2014	3/1/2014	ACOMS	Completed	3/12/2014	N		Michael Ortwerth michael.ortwerth@fda.hhs.gov
239	XI-C	1142	(c)	NO	NA	FDA shall issue guidance describing how it reviews financial interests that do not meet the statutory definition of a disqualifying interest under section 208 of Title 18, United States Code for the purposes of participating in a particular matter	Draft Guidance	—	12/31/2014	12/31/2014	ACOMS	In process, on track to meet due date	—	Y		Michael Ortwerth michael.ortwerth@fda.hhs.gov

** Target dates are used for internal management purposes and are based on knowledge of resources at the time and are subject to change
*** Current Status reflects status of deliverable in relation to meeting Target Completion Date

FOOD AND DRUG SAFETY AND INNOVATION ACT (FDASIA) INTERNAL TRACKING SHEET

* User Fee Commitment Letter deliverables are identified using the following Section numbers: PDUFA - 100, MDUFA - 200, GDUFA - 300, BSUFA - 400. User Fee deliverables do not have "statutory" dates and the dates represent agreements in the Commitment Letters.

Item #	Title	Section *	Sub-Section	UFA Goals Letter	Goals Letter Citation	Deliverable Description	Deliverable Type	Statutory Deadline *	Targeted Completion Date **	FDA Completion Due Date **	Responsible Organization	Status ***	Date Completed	Publicly Tracked? (FDASIA-TRACK)	FDASIA TRACK Notes (Will be posted on public FDA-TRACK Website)	Public Website Contact
240	XI-C	1142		NO	NA	(* No statutory language *) Update 3 existing Guidance documents for Advisory Committees to conform to changes in the FD&C Act enacted as part of FDASIA	Draft and Final Guidances	--	5/31/2014		ACOMS	In process on track to meet due date	--	Y	1. Update Guidance on "Public Availability of Advisory Committee Members' Financial Interest Information and Waivers" to conform to changes in the FD&C Act enacted as part of FDASIA (target date 3/30/2014) 2. Update Guidance on "The Open Public Hearing at FDA Advisory Committee Meetings" to conform to changes in the FD&C Act enacted as part of FDASIA (completed 5/15/2013) 3. Update Guidance on "Procedures for Determining Conflict of Interest and Eligibility for Participation in FDA Advisory Committees" to conform to changes in the FD&C Act enacted as part of FDASIA (target date 5/31/2014)	Michael Ortwerth michael.ortwerth@fda.hhs.gov
241	XI-D	1152		NO		Amends the Controlled Substances Act to add synthetic cannabinoids and other synthetic substances to Schedule I of the CSA	Other	--	--		DOJ, CDER	Scheduled to begin later	--	N		

** Target dates are used for internal management purposes and are based on knowledge of resources at the time and are subject to change.
*** Current Status reflects status of deliverable relative to meeting Target Completion Date.

FRED UPTON, MICHIGAN
CHAIRMAN

HENRY A. WAXMAN, CALIFORNIA
RANKING MEMBER

ONE HUNDRED THIRTEENTH CONGRESS

Congress of the United States

House of Representatives

COMMITTEE ON ENERGY AND COMMERCE

2125 RAYBURN HOUSE OFFICE BUILDING
WASHINGTON, DC 20515–6115
Majority (202) 225–2927
Minority (202) 225–3641

December 17, 2013

Dr. Jeffrey E. Shuren
Director
Center for Devices and Radiological Health
U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

Dear Dr. Shuren:

Thank you for appearing before the Subcommittee on Health on Friday, November 15, 2013, to testify at the hearing entitled "Reviewing FDA's Implementation of FDASIA."

Pursuant to the Rules of the Committee on Energy and Commerce, the hearing record remains open for ten business days to permit Members to submit additional questions for the record, which are attached. The format of your responses to these questions should be as follows: (1) the name of the Member whose question you are addressing, (2) the complete text of the question you are addressing in bold, and (3) your answer to that question in plain text.

Also attached are Member requests made during the hearing. The format of your responses to these requests should follow the same format as your responses to the additional questions for the record.

To facilitate the printing of the hearing record, please respond to these questions and requests by the close of business on Thursday, January 9, 2014. Your responses should be mailed to Sydne Harwick, Legislative Clerk, Committee on Energy and Commerce, 2125 Rayburn House Office Building, Washington, D.C. 20515 and e-mailed in Word format to **Sydne.Harwick@mail.house.gov**.

Thank you again for your time and effort preparing and delivering testimony before the Subcommittee.

Sincerely,

Joseph R. Pitts
Chairman
Subcommittee on Health

cc: The Honorable Frank Pallone, Jr., Ranking Member, Subcommittee on Health

Attachments

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

The Honorable Joseph R. Pitts
Chairman
Subcommittee on Health
Committee on Energy and Commerce
House of Representatives
Washington, D.C. 20515-6115

NOV 12 2014

Dear Mr. Chairman:

Thank you for providing the Food and Drug Administration (FDA or the Agency) with the opportunity to testify at the November 15, 2013, hearing before the Subcommittee on Health, Committee on Energy and Commerce, entitled "Reviewing FDA's Implementation of FDASIA." This is a response for the record to questions posed by you and other Committee Members to Dr. Jeffrey E. Shuren in a letter we received on December 17, 2013. We are also responding to questions posed by you and Representative Capps at the hearing.

Please let us know if you have any further questions.

Sincerely,

Thomas A. Kraus
Associate Commissioner
for Legislation

cc: The Honorable Frank Pallone, Jr.
Ranking Member
Subcommittee on Health
Committee on Energy and Commerce

We have restated each Member's questions below in bold, followed by our responses.

The Honorable Joseph R. Pitts

1. **Please describe how the FDA was involved in setting the parameters of the assessment between industry and the FDA that objectively assess the FDA's Premarket review process. Please submit a detailed accounting of the agency's involvement with the contractor relating to the review and any recommendations or direction you provided.**

INTRODUCTION

Pursuant to the Performance Goals and Procedures[1] adopted under the 2012 Medical Device User Fee Amendments[2] (MDUFA III), FDA agreed to participate with the device industry in a comprehensive assessment of the process for the review of device applications (the Independent Assessment). This requirement is to conduct a comprehensive assessment by an independent consulting firm of FDA premarket review processes for medical devices and to identify opportunities for improvement that will significantly impact the review of device premarket applications.[3]

In Phase 1 of the Independent Assessment, FDA and the medical device industry participated in the comprehensive assessment of the process for the review of medical device submissions. The Agency analyzed the recommendations of the assessment and implemented selected actions and incorporated selected outcomes of the assessment into a Good Review Management Practices guidance document.

Primary objectives of Phase 1 of the Independent Assessment included:

- Identification of best practices and prioritization of process improvements for conducting predictable, efficient, and consistent premarket reviews that meet regulatory review standards;
- In-depth analyses of the elements of the review process, in order to identify best practices and opportunities for improvement, including root-cause analyses of selected significant factors;
- Assessment of resource allocation to premarket device reviews across FDA;
- Development of implementation plans for selected recommendations; and
- Development of metrics to ensure successful implementation of recommendations and demonstrate achievement of expected results.

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[1] This document is commonly referred to as the "MDUFA III Commitment Letter" and is available on FDA's public website at http://www.fda.gov/downloads/medicaldevices/newsevents/workshopsconferences/ucm295454.pdf.

[2] Title II of the Food and Drug Administration Safety and Innovation Act, Public Law 112-144 (126 Stat. 993) (July 9, 2012) is available at http://www.gpo.gov/fdsys/pkg/PLAW-112publ144/pdf/PLAW-112publ144.pdf.

[3] The contract for the Independent Assessment contemplates a three-year performance period, from March 31, 2013, through February 1, 2016. The performance period for Phase 1 is March 31, 2013–September 30, 2014, and the performance period for Phase 2 is October 1, 2014–February 29, 2016.

Phase 2 of the Independent Assessment required the contractor to evaluate the implementation of recommendations adopted under Phase 1 and publish a written assessment of FDA's implementation of those recommendations. This was published on June 11, 2014.

FDA INVOLVEMENT IN THE INDEPENDENT ASSESSMENT

Upon enactment of FDASIA[4] in July 2012, FDA established a Project Advisory Group (PAG), comprised of high-level policy staff, to advise the Independent Assessment process, which held its Kickoff Meeting on July 12, 2012. A Technical Advisory Group (TAG), comprised of technical-level subject matter experts, was also established. The first meeting of the Independent Assessment TAG was held on September 12, 2012. The TAG drafted an initial Statement of Work,[5] which was reviewed and approved by the PAG, and in December 2012, FDA published a notice in the *Federal* Register,[6] soliciting public comments on the draft Statement of Work for the Independent Assessment.

The Agency received comments[7] from the device industry and other interested stakeholders in response to the *Federal Register* notice. In addition, on January 29, 2013, the Agency spoke with industry representatives regarding the feedback received about the draft Statement of Work. FDA took those comments and input into account when finalizing the Statement of Work[8] for the Independent Assessment on March 25, 2013.

On April 19, 2013, FDA issued the Request for Proposal for the Independent Assessment.

On June 11, 2013, FDA awarded the task order for the Independent Assessment to Booz Allen Hamilton, Inc. (BAH). BAH fully meets the qualification requirements stated in the Commitment Letter and has a solid record of successfully completing this type of assessment for other FDA user fee programs. The period of performance for the contract for the Independent Assessment began on June 11, 2013.

On July 1, 2013, FDA and BAH held a kick-off meeting for the Independent Assessment at FDA's headquarters in Silver Spring, Maryland. At the kick-off meeting, BAH introduced its team to the FDA PAG and TAG and laid out its technical approach to the Assessment, including the project's objectives and schedule.

As specified in the Statement of Work, BAH developed a project work plan to accomplish the requirements of the Statement of Work. That work plan identifies the

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[4] MDUFA III was enacted as Title II of the Food and Drug Administration Safety and Innovation Act, or FDASIA.
[5] The draft Statement of Work (dated Dec. 14, 2012) is available on FDA's public website at http://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/overview/mdufaiii/ucm331516.pdf.
[6] FDA. "Comprehensive Assessment of the Process for the Review of Device Submissions: Request for Comments." Docket No. FDA-2012-N-1202, 77 *Fed. Reg.* 75173 (Dec. 19, 2012), available at http://www.gpo.gov/fdsys/pkg/FR-2012-12-19/pdf/2012-30511.pdf.
[7] Copies of the public comments that were submitted are available at regulations.gov at http://www.regulations.gov/#!documentDetail;D=FDA-2012-N-1202-0001.
[8] The scope and requirements of the Independent Assessment are described in detail within the final Statement of Work, which is available on FDA's public website at http://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/overview/mdufaiii/ucm376252.pdf.

sources, methods, and metrics to be included in the analysis; specifies the schedule of deliverables, including FDA review time of draft materials; details the sources, methods, and metrics to be used; identifies the project personnel and organizational structure; and explains the procedures to be followed to ensure proper communications, reporting, and project management controls.

BAH delivered its draft work plan for the Independent Assessment to FDA on July 19, 2013. FDA provided feedback regarding the draft work plan at a meeting held in Silver Spring, Maryland, on July 25, 2012, and BAH's final work plan for the Independent Assessment was received by the Agency on August 2, 2013.

Since July 2012, FDA has provided quarterly updates to industry and interested stakeholders on the progress being made in the conduct of the Independent Assessment. These updates, which are publicly available on the Agency's website, are provided as part of FDA's commitment in MDUFA III to provide detailed quarterly reports on the Agency's progress toward meeting the goals described in the MDUFA III Commitment Letter.[9] After the contract was awarded, at the July 30, 2013, quarterly MDUFA III update meeting between FDA and industry representatives, BAH introduced its team and outlined its planned approach to the assessment.

The conduct of the Independent Assessment contemplates that FDA (and industry) will participate in the Independent Assessment process, and that FDA (and industry) will be consulted during the course of that process.[10]

Progress reports and updates from BAH's assessment team are ongoing. BAH delivers written progress and financial reports to the FDA Contracting Officer's Representative (COR)[11] on a monthly basis. In addition, BAH makes oral presentations to FDA's PAG and TAG on each major report or plan deliverable prior to delivery. These presentations are scheduled by the FDA COR, and BAH is responsible for drafting minutes for each such meeting. In addition, bi-weekly progress reports are provided by BAH to the FDA COR via e-mail and in person. As of November 15, 2013, nine bi-weekly status reports had been provided to the FDA COR, and seven in-person meetings had been held.

On November 15, 2013, BAH delivered to FDA a working draft document with the contractor's preliminary findings and high-priority recommendations for the Independent Assessment, including data collected and sources, to allow FDA to verify the accuracy of the data and assumptions. The final written report on BAH's high-priority recommendations was delivered to FDA on December 6, 2013, and FDA posted that

[9] See, e.g., "MDUFA III Quarterly Performance Update: Independent Assessment of Medical Device Review Process – 4th Quarter FY 2013 Status" (Nov. 5, 2013), available at http://www.fda.gov/medicaldevices/deviceregulationandguidance/overview/medicaldeviceuserfeeandmodernizationact mdufma/ucm109210.htm.

[10] The Commitment Letter specifically states that "FDA and the device industry will participate in a comprehensive assessment of the process for the review of device applications. The assessment will include consultation with both FDA and industry." The final Statement of Work for the Independent Assessment specifies that interviews by BAH personnel with FDA medical device review staff, as well as observation of meetings between FDA and industry, are to comprise part of the data and information-gathering process.

[11] The COR serves as the liaison between FDA and BAH.

report on the Agency's public website on December 11, 2013. A copy of the report is available at *http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/Overview/MDUFAIII/UCM378202.pdf*.

NEXT STEPS IN THE INDEPENDENT ASSESSMENT PROCESS

In May 2014, FDA issued the Agency's Implementation Plan for the high-priority recommendations that were reported by BAH in December 2013. In June 2014, BAH issued its Final Report, which included the contractor's complete findings and recommendations for Phase 1 of the Independent Assessment. Phase 1 of the Independent Assessment will conclude in December 2014, when FDA issues the Agency's Implementation Plan for BAH's final recommendations.

The Phase 2 Final Evaluation Report for the Independent Assessment is scheduled to be posted on the FDA public website by February 1, 2016.

2. In your testimony, you note that you are making significant progress in implementing FDASIA and meeting most due dates. Which due dates are you missing and when will they be completed?

Section 604 of FDASIA added section 510(n)(2) to the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 USC 360(n)(2)). This new provision requires the Secretary of Health and Human Services to submit to the House of Representatives' Committee on Energy and Commerce (E&C Committee) and the Senate Committee on Health, Education, Labor, and Pensions (HELP Committee) a report on when a premarket notification under section 510(k) of the FD&C Act should be submitted for a modification or change to a legally marketed device ("Modifications Report"). On June 13, 2013, FDA held a full-day public meeting, "510(k) Device Modifications: Deciding When to Submit a 510(k) for a Change to an Existing Device." At this meeting of more than 1,200 registrants, representatives from FDA and interested stakeholders discussed the Agency's policy and the current regulations concerning when a modification made to a 510(k)-cleared device requires a new 510(k) submission. FDA carefully considered the discussion at the public meeting and comments submitted to the docket in drafting the Modifications Report. The statutory deadline for submission of the Modifications Report to the E&C and HELP Committees was January 9, 2014. The report was sent to Congress on February 25, 2014.

As directed by Congress, in section 618 of FDASIA, FDA, in consultation with the Federal Communications Commission (FCC) and the Office of the National Coordinator for Health Information Technology (ONC), is working toward publishing a report containing a proposed strategy and recommendations on an appropriate, risk-based regulatory framework for health information technology (Health IT) that promotes innovation, protects patient safety and avoids regulatory duplication (Health IT Report). In 2013, FDA, in collaboration with ONC and FCC, created a working group (the "FDASIA Workgroup") of external stakeholders and experts under ONC's Health IT

Policy Committee. FDA, ONC, and FCC intend to use the input from ONC's Health IT Policy Committee, which adopted in full the FDASIA Workgroup's recommendations, in the development of the Health IT Report. Although the Health IT Report was due to be posted on the websites of FDA, FCC and ONC by January 9, 2014, the three agencies needed additional time to allow for careful consideration of the FDASIA Workgroup's recommendations adopted by ONC's Health IT Policy Committee and other public input. This report was completed on April 1, 2014.

3. **The FDA appears to not have revised its 1994 strategy document on reviewing and finalizing the regulatory status of pre-amendment Class III devices based on the changes made in the law by FDASIA last year. Since FDASIA made significant changes in the sections of the law governing the processes by which the Agency goes about considering the revision of pre-amendment Class III devices, when does the Agency plan to revise this outdated document, and, in the meantime, what steps has the Agency taken to ensure that all of the new process requirements of FDASIA (especially sections 515(i) and 515(b)) are being met as pre-amendment Class III devices move through the revision/reclassification process?**

Section 608 of FDASIA changed the procedures for requiring premarket approval for preamendments Class III devices ("call for PMAs") under section 515(b) of the FD&C Act, 21 U.S.C. § 360e(b), and for reclassifying devices under section 513(e) of the FD&C Act, 21 U.S.C. § 360c(e), from a rulemaking to an administrative order process, and added a requirement for review by a device classification panel (panel). Section 608 of FDASIA revised section 515(i) of the FD&C Act, 21 U.S.C. §360e(i), to reflect the new administrative order process; however, FDASIA did not otherwise change the process or add any additional steps to the FD&C Act. Congress did not comment during the enactment of FDASIA on FDA's long-standing process for addressing the remaining types of preamendments Class III devices, for which there has not been a call for PMAs (by either calling for PMAs or reclassifying into Class I or II), other than to suggest that FDA act expeditiously to do so.[12]

Congress[13] and GAO[14] have urged FDA to address the issue of preamendments Class III devices,[15] for which there has not been a call for PMAs in an expeditious manner, and the

[12] H. Rep. 112-495 (2012) at 28.

[13] See the legislative history of the Safe Medical Devices Act (SMDA) of 1990. The Senate report makes clear the need to require submission of PMAs as soon as possible for those devices that are to remain in Class III, stating "...it is of profound importance to the Committee that the revision of classifications and the regulations requiring PMAs be completed as quickly as possible" (S. Rept. 513, 101st Cong., 2d sess. 18 (1990)). In addition, the House of Representatives Report states that when formulating the schedules for requiring the submission of the PMAs, FDA should take into account its priorities and limited resources, together with the Committee's intention that the evaluation of the process be expeditious (H. Rept. 808, 101st Cong., 2d sess. 26 (1990)).

[14] In January, 2009, the Government Accountability Office (GAO) issued a report, Government Accountability Office (GAO) (09-190), FDA Should Take Steps to Ensure that High-Risk Device Types are Approved through the Most Stringent Premarket Review Process. This report recommended that "FDA expeditiously take steps to issue regulations for Class III device types currently allowed to enter the market via the 510(k) process." GAO further stated that "[t]hese steps should include issuing regulations to (1) reclassify each device type into Class I or Class II, or requiring it to remain in Class III, and (2) for those device types remaining in Class III, require approval for marketing through the PMA process."

Agency has taken many actions in order to promptly and efficiently address this issue in a transparent and predictable manner. These actions include, among others, the publication of a notice in the *Federal* Register,[16] describing FDA's strategy for implementation of the SMDA, P.L.101-629 (1994 strategy document) and the 515 Program Initiative (discussed below).

The process described in the 1994 strategy document was created to carry out Congress' intent.[17] It established an efficient means to review the regulatory status of the remaining 117 preamendments Class III devices, for which FDA had not yet initiated any action to call for PMAs while providing ample opportunity for public participation, in accordance with applicable law and regulation. FDA made significant progress on addressing the preamendments Class III devices, for which there had not been a call for PMAs since publishing the 1994 strategy document; however, as of 2009, 26 preamendments Class III device types still had not been reclassified or had a call for PMAs. Therefore, in 2009, FDA implemented the 515 Program Initiative to further facilitate a transparent review of the remaining 26 preamendments Class III device types still requiring additional Agency action. FDA developed a five-step process for finalizing the classification of preamendments device types and publicized the process on the Agency's 515 Program Initiative web page at *http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDRH/CDRHTransparency/ucm240310.htm* (515 initiative page). FDA also publicly tracks the status of the remaining device types that needed to be addressed on the 515 Project Status web page at *http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDRH/CDRHTransparency/ucm240318.htm* (515 status page).

Since late 2009, when FDA began the 515 Program Initiative, FDA has made substantial progress in reclassifying or calling for PMAs for the 26 remaining types of preamendments Class III devices. As of January 17, 2014, FDA has either issued a proposed or final order for 21 of the 26 remaining device types. In addition, FDA has issued two proposed rules that have yet to be reissued as proposed orders, as required by FDASIA.[18] Significantly, for 25 of the 26 device types, FDA has taken at least one of three major regulatory actions—proposed reclassification or called for PMAs; held a panel meeting; or issued a final reclassification or called for PMAs.

FDA continues to focus resources on expeditiously and transparently completing the process for the remaining device types that allows for multiple opportunities for public

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[15] A preamendments Class III device is a Class III device that was introduced or delivered for introduction into interstate commerce for commercial distribution prior to the passage of the Medical Device Amendments of 1976, or is of a type so introduced or delivered and is substantially equivalent to another device within that type (see section 515(b) of the FD&C Act, 21 U.S.C. § 360e(b).

[16] 59 Fed. Reg. 23731 (May 6, 1994).

[17] See footnote 2.

[18] FDASIA required FDA to issue six proposed orders for device types, for which proposed rules for preamendments Class III devices had already been issued but not finalized. FDA has moved forward and has already re-proposed four of the six actions as proposed orders.

participation. The Agency has taken the following steps to ensure timely completion of this effort:

- The 515 initiative page and the 515 status page have been revised to capture the changes from FDASIA, and the 515 status page is updated each time an action is taken regarding one of the remaining device types (e.g., panel meetings, proposed orders, and final orders). Since FDASIA's enactment, FDA has issued proposed orders for 14 preamendments Class III device types, five of which have been finalized.

- On March 25, 2014, the Agency published the Medical Device Classification and Reclassification Procedures proposed rule, proposing changes to its reclassification process to conform to the new, streamlined procedures FDASIA required. FDA is also proposing to clarify the criteria for Class III (high-risk) devices. The proposed clarifications should promote transparency in our risk-based regulation and provide insight into the level of regulatory control necessary to address their risks. Clear regulations increase the predictability, transparency, and consistency of Agency actions. A general update to FDA's medical device classification regulation will increase certainty about how devices will be regulated, benefitting industry, device users, and FDA staff.

- Senior management within the Center for Devices and Radiological Health is regularly briefed on the status of the remaining preamendments Class III device types, for which there has not been a call for PMAs, so that they may guide and monitor the process.

In short, FDA is working diligently to complete the task it began in 2009. Upon completion, the 1994 strategy document will no longer be relevant. FDA does not believe diverting resources from this important task to make changes to the 1994 strategy document is currently warranted.

4. **As you know, in the Safe Medical Devices Act of 1990 Congress added a new subsection to Section 515 (i.e. Section 515(i)) to address the situation created by the failure of the Agency to resolve the classification issues associated with pre-amendment Class III devices. As you also know, these pre-amendment devices are devices about which FDA was uncertain how to classify when the classification system first began. However, most of these devices have been going to market through the 510(k) market notification process for decades. The purpose of this new subsection was to provide a clear path to revise the classification of this special category of devices either into Class I or Class II, or, if required, keep the device in Class III.**

   A part of this Section 515(i) (i.e. Section (515(i)(3)) clearly states that when this process of revision is completed if the device is to remain in Class III, "The Secretary shall...establish a schedule for the promulgation of a subsection (b) of this section ...." Again, as you well know, this subsection (b) refers to a different

subsection and establishes the basis for requiring a Pre-Market Approval (PMA).

To resolve the final disposition of these pre-amendment Class III devices, especially if the FDA was proposing to regulate them as Class III devices, Congress authorized a two-step process:

Step 1 - (or Section 515(i)) - Revise the classification of the device to either a Class I or Class II, or decide that it must be regulated as a Class III device, and if it is to be a Class III device, then

Step 2 - (or Section 515(b)) - Require that the device have an approval of an application for a pre-market approval.

I have three questions that pertain to the Agency's Proposed Order for Automatic External Defibrillators (AEDs) issued on March 25, 2013:

a. Has the Agency ever issued a Proposed Order as required by Section 515(i)(2)? If no, why not? If yes, please provide.

b. Has the Agency ever issued the "schedule for the promulgation of a subsection (b) of this section..." as required by Section 515(i)(3)? If no, why not? If yes, please provide.

c. On what legal basis does the Agency justify conflating into one step the Congressionally mandated two-step process involved in the Section 515(i) and 515(b) requirements (or perhaps just omitting the Section 515(i)(2) and (3) requirements altogether and going straight to the Section 515(b) requirements) as it appears to have done in the March 25th Proposed Order?

As discussed in the answer above, section 608 of FDASIA amended the procedures for a call for PMAs under section 515(b) of the FD&C Act, 21 U.S.C. § 360e(b), and reclassifying devices under section 513(e) of the FD&C Act, 21 U.S.C. § 360c(e), from rulemaking to an administrative order process and added a requirement for a panel review but did not otherwise change the process or add any additional steps to the FD&C Act or affect FDA's long-standing process for addressing preamendments Class III devices, for which there has not been a call for PMAs. FDASIA made similar changes to section 515(i) of the FD&C Act to be consistent with the administrative order process, but the process was not otherwise changed. Congress did not comment during the enactment of FDASIA on FDA's long-standing process for addressing the remaining preamendments Class III devices in this category, other than to suggest that FDA act expeditiously to do so.[19] FDA, therefore, implemented section 608 of FDASIA by adapting its long-standing process to the order process FDASIA mandated.

[19] H. Rep. 112-495 (2012) at 28

As discussed above, after enactment of the SMDA, FDA published the 1994 strategy document[20] to describe the Agency's strategy for implementing the provisions of the SMDA, addressing Class III preamendments devices, for which there had not been a call for PMAs. FDA stated in the 1994 strategy document that "the SMDA does not prevent FDA from proceeding immediately to rulemaking under section 515(b) of the [FD&C Act] on specific devices, in the interest of public health, independent of the procedure in section 515(i) of the [FD&C Act]."[21] The Agency also implemented the 515 Program Initiative in 2009. FDA lays out the five-step process for addressing the remaining preamendments Class III devices, for which there has not been a call for PMAs on the Agency's 515 initiative page, and publicly tracks the status of the remaining device types in this category on the 515 status page.

As you note, devices within a preamendments Class III type may be cleared through the less-stringent 510(k) process, unless and until FDA calls for PMAs; if FDA reclassifies them into Class II they may continue to be cleared through the 510(k) process. FDA's procedures for addressing the remaining preamendments Class III devices subject only to 510(k), including AEDs, is consistent with the FD&C Act and long-standing Agency practices, provides full and fair opportunity for interested persons, including manufacturers, patients, health care professionals, other members of the general public, and experts, to comment on a proposed reclassification or call for PMAs, and ensures that FDA may continue to expeditiously work to address all remaining preamendments Class III device types that are currently permitted to utilize the 510(k) process to enter the market. The process, as revised to be consistent with FDASIA, provides multiple opportunities for public input. For example for Automated External Defibrillators (AEDs):

1995 515(i) Order:[22] FDA published a 515(i) order in 1995 regarding certain preamendments Class III devices. The order required manufacturers of these devices to submit safety and effectiveness information to FDA. Included in this order were arrhythmia detectors and alarms. At the time, AEDs were considered part of the arrhythmia detectors and alarms device type because AEDs were found substantially equivalent to these devices. Prior to 2003, both AEDs and the arrhythmia detectors and alarms were Class III devices.

2002 Proposed Rule:[23] FDA issued a proposed rule in 2002 to reclassify arrhythmia detector and alarms from Class III to Class II with special controls. This action was taken in response to reclassification petitions requesting that arrhythmia detectors and alarms be reclassified. In this proposed rule, FDA announced that although the Agency was proposing to reclassify arrhythmia detectors and alarms to Class II, FDA was proposing to retain AEDs in Class III and establish a separate AED classification. The proposed

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[20] 59 Fed. Reg. 23731 (May 6, 1994). This strategy also is available on FDA's website at http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm081251.htm.
[21] 59 Fed. Reg. 23731, 23731.
[22] 60 Fed. Reg. 41984 (Aug. 14, 1995).
[23] 67 Fed. Reg. 76706 (Dec. 13, 2002).

rule also stated that FDA would address, at a later date, the possible reclassification of AEDs.

2003 Final Rule:[24] FDA issued a final rule that reclassified arrhythmia detector and alarms from Class III to Class II and established a separate classification regulation retaining AEDs in class III (see 21 CFR 870.5310). In addition, this final rule reiterated the comment made in the proposed rule about addressing, at a later date, the possible reclassification of AEDs. In the same *Federal Register* issue as this final rule, a Notice of Intent was published[25] requesting information concerning the safety and effectiveness of AEDs.

2009 515(i) Order:[26] FDA issued a 515(i) order in 2009 for certain preamendments Class III devices, including AEDs. This order required manufacturers to submit to FDA a summary of any information known or otherwise available to them, including adverse safety or effectiveness information. FDA considered the information received in response to the 515(i) order in determining whether to call for PMAs or to reclassify the devices that were the subject of the order, including AEDs.

January 25, 2011 Panel Meeting: FDA convened a meeting of the Circulatory System Devices Panel (the AED panel), which was open to the public. Interested persons were provided the opportunity to present data, information, or views, orally or in writing, on the issues pending before the AED panel.[27] A number of AED manufacturers had the opportunity to present their recommendation for reclassifying AEDs. FDA also presented its analysis of the proper classification for AEDs. The AED panel discussed and made recommendations on whether AEDs should remain Class III (subject to premarket approval) or be reclassified to Class II (subject to special controls and general controls including premarket notification). A significant majority of the AED panel recommended that AEDs remain in Class III and subject to PMA requirements. The AED panel reached this conclusion because insufficient information exists to determine that general and special controls would provide a reasonable assurance of safety and effectiveness and AEDs are lifesaving devices. Moreover, AEDs have a significant history of adverse events and recalls. This adverse event history indicates existing controls were not adequately mitigating the risks associated with AEDs and, therefore, are likely insufficient to provide a reasonable assurance of safety and effectiveness. The AED panel meeting transcript and other meeting materials are available to the public on FDA's website at *http://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/MedicalDevices/MedicalDevicesAdvisoryCommittee/CirculatorySystemDevices*.

March 2013 Proposed Order:[28] In this proposed order, FDA announced its intention to call for PMAs for the AED device, including its accessories (i.e., pad electrodes,

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[24] 68 Fed Reg 61342 (Oct. 28, 2003).
[25] 68 Fed. Reg. 61446 (Oct. 28, 2003).
[26] 74 Fed. Reg. 16214 (Apr. 9, 2009).
[27] 75 Fed. Reg. 81282 (Dec. 27, 2010).
[28] 78 Fed. Reg. 17890 (Mar. 25, 2013).

batteries, and adapters). As required by section 515(b) of the FD&C Act, as amended by FDASIA, the proposed order provides its proposed findings regarding (1) the degree of risk of illness or injury designed to be eliminated or reduced by requiring that this device have premarket approval, and (2) the benefits to the public from use of the device. These findings are based on the reports and recommendations of the AED panel for the proper classification of these devices, along with information submitted in response to the 2009 515(i) order and any additional information that FDA obtained since convening the AED panel.

In accordance with section 515(b)(2)(D) of the FD&C Act, 21 U.S.C. 360e(b)(2)(D), FDA provided an opportunity in the proposed order for interested persons to submit a request for a change in classification of AEDs. FDA opened a docket for interested persons to submit comments or request a change in classification in response to the proposed order.

The comment period closed on June 24, 2013. FDA received more than 50 comments to the proposed order, including one request for a change in classification. FDA also engaged with AED manufacturers to discuss the proposed order. FDA will consider the request for a change in classification and all comments to the proposed order before issuing any final administrative order.

5. **The only legislative history for what became FDASIA Section 608 is language that was drafted and adopted by this Committee. As you know, in the original House version of the bill, no changes were made to the reclassification provisions in Sections 515(i) and 515(b). As a result, this legislative history is relevant only to the original pre-FDASIA reclassification process. Given the absence of a legislative history pertaining to the changes in this section of the law ultimately passed by Congress, the actual legislative language itself controls.**

   FDASIA states that an order requiring PMA cannot become final until three events occur in the following order, as listed in Section 608: a proposed order, a panel, and a response to comments on the order. In the case of AEDs, based on the Agency's March 25, 2013 proposed order, the Agency appears to take the position that it can remove the panel from this sequence, and that Congress did not intend the sequence that is explicitly listed in the statutory language. Specifically, the FDA appears to rely on a panel meeting that occurred over 18 months before the enactment of FDASIA. Given the fact that in FDASIA Congress granted the Agency a new authority to revise and reclassify pre-amendment devices based on a final order rather than rulemaking, and that the only guidance on this new language is what exists in the statute itself, on what basis does the Agency believe it has the authority to ignore the sequence listed in the statute?

As stated above, FDASIA did not grant FDA new authority to call for PMAs and reclassify preamendments Class III devices. FDASIA simply amended the existing

authorities to replace the rulemaking process with an administrative order process and mandated review by a device classification panel. Section 515(b) of the FD&C Act, as amended by section 608 of FDASIA, sets out the following critical steps in the process to require premarket approval for a preamendments Class III device, stating that FDA may do so:

> by administrative order following publication of a proposed order in the *Federal Register*, a meeting of a device classification panel described in section 513(b), and consideration of comments from all affected stakeholders . . .

This provision makes clear that issuance of a proposed order and a meeting of a device classification panel must precede issuance of a final administrative order, but does not prescribe the order of the panel meeting relative to issuance of the proposed order. Therefore, this provision provides the Agency with the flexibility to hold a panel meeting either before or after the issuance of a proposed order. Whether the panel meeting takes place before or after the proposed order, interested parties will have an opportunity to participate in accordance with FDA regulations and policies governing the panels.

The benefits in efficiency created when a proposed reclassification or call for PMAs reflects the input of FDA's expert panels may explain why the FD&C Act mandates that the panel meeting occur *before* issuance of the proposed classification regulation for initial classifications of devices.[29] Further, although the FD&C Act did not mandate a meeting of an advisory panel for reclassifying or calling for PMAs for devices prior to the enactment of FDASIA,[30] when FDA held panel meetings associated with such actions, the meetings would often occur before any proposal issued.

Convening a panel meeting prior to the issuance of a proposed order for a preamendments Class III device allows FDA to receive advice and recommendations from the panel on the appropriate regulatory action for the device (i.e., reclassification or call for PMAs) and also provides the public an opportunity to present its views on this topic prior to FDA formulating a proposal and utilizing the Agency's resources to issue a proposed order. In many cases, the interests of regulated industry and the general public may be best served by ensuring FDA receives expert input *before* issuing a proposed order. When the appropriate regulatory action for a preamendments Class III device is unclear, the opinions of FDA's expert panel members are an important part of the record that FDA relies upon in determining whether a preamendments Class III device should be reclassified or should be subject to premarket approval. When FDA issues a proposed order without the benefit of panel input, there is an increased likelihood of a conflict between the panel's recommendation and the proposed order and, therefore, a higher probability that FDA may reconsider its proposed order or even have to issue a new

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[29] See 513(d)(1) of the FD&C Act, 21 U.S.C. § 360c(d)(1).

[30] Former section 515(b) of the FD&C Act, however, required FDA to consult with the appropriate panel, if a request for reclassification was received within 15 days of issuance of a proposed rule calling for PMAs. Former section 513(e) of the FD&C Act provided for FDA, at its discretion, to secure a panel recommendation prior to the promulgation of a reclassification rule. Prior to FDASIA, when a panel meeting was discretionary, FDA oftentimes held a panel meeting prior to proposing reclassification for a device, for example, when the Agency determined that a recommendation from the panel would help inform whether proposing reclassification for the device was appropriate.

proposed order. Such an outcome would not only further delay completion of the final action (i.e., either reclassification or call for PMAs) for preamendments Class III devices and needlessly expend scarce FDA resources, but would create uncertainty for manufacturers and for the public.

For AEDs, FDA has followed its long-standing practice described above for preamendments Class III devices, for which there has not been a call for PMAs. The findings in the March 2013 proposed order are based on the reports and recommendations of the January 2011 AED panel for the proper classification of these devices, with information submitted in response to the 2009 515(i) order, and any additional information that FDA obtained since convening the AED panel. In accordance with section 515(b)(2)(D) of the FD&C Act, 21 U.S.C. 360e(b)(2)(D), FDA provided an opportunity in the proposed order for interested persons to submit a request for a change in classification of AEDs. FDA also opened a docket for interested persons to submit comments or request a change in classification in response to the proposed order. FDA will review and consider all comments made in response to the issuance of the proposed order, and will also consider the request for a change in classification that the Agency received before taking any further action.

The Honorable Leonard Lance

1. **As you may be aware, I have authored legislation, the FDA Safety Over Sequestration (FDA SOS) Act, which would protect the FDA user fees from the threat of sequester, should Congress face a similar budget situation as we did earlier this year. This legislation is supported by many of my colleagues on this committee on both sides of the aisle and it is our hope that it be considered and passed soon in order to maintain predictability in the review process, as well as incentive to continue to engage in these agreements.**

   OMB unfortunately interpreted sequestration to apply equally to both FDA appropriations and industry user fees. As a result, more than $80 million in private user fee funding is being sequestrated in an agency account where they cannot be spent or put to any practical purpose. The FDA Safety Over Sequestration (FDA SOS) Act would clarify that industry user fees cannot be sequestered. From the perspective of a senior FDA manager, what impacts is the sequestration of user fees having on FDA operations, regulatory science, and product evaluation? Would you support passage of the FDA SOS bill?

As Commissioner Hamburg has said, an agency as important as FDA needs predictability, and cannot be run well if you don't know what budget you'll be given during the year, or if you do not know whether or not you can draw from certain resources. The administration has not taken a position on this bill. The sequester restricted access to an estimated $79 million in user fees in FY 2013. Sponsors paid fees for specific commitments that were negotiated as part of the Prescription Drug User Fee Act (PDUFA), Medical Device User Fee Amendments (MDUFA), Generic Drug User

Fee Act (GDUFA), Biosimilar User Fee Act (BsUFA), Animal Drug User Fee Act (ADUFA), and Animal Generic Drug User Fee Act (AGDUFA) agreements, but FDA did not have access to the full FY 2013 amounts of the funds due to the sequestration. Sequestration impacts FDA's ability to meet these commitments, such as the program enhancements specified in the PDUFA V and MDUFA III commitment letters. This work must be done by FDA, not other FDA constituencies. Many of these enhancements will have long-term benefits for the public health. The delay of these enhancements resulting from the sequester will postpone these benefits. If sequestration is mitigated in FY 2014 and future years, FDA will have enhanced capacity to meet its commitments to industry and the public.

2. **Briefly, how are Agency operations impacted by sequestration? As a result, how are you absorbing these cuts?**

Previously, we estimated the overall sequestration of user fees to be $85M. The estimate for sequestration as of September 30, 2013, is $79M. Of that amount, $54M is attributable to PDUFA, GDUFA, BsUFA, and MDUFA. The reason for the change in sequestration amounts is that actual collections were different from the estimates at the beginning of the year.

The FY 2013 sequestration and rescission reductions have harmed FDA's ability to protect the public and ensure the safety of America's food and medical products. FDA has been unable to hire to the appropriate staffing level for its workload. This reduced staffing level has:

- delayed FDA's ability to conduct regulatory review and issue regulations and guidance
- impaired FDA's ability to conduct inspections in a timely manner
- reduced FDA's capability to conduct relevant regulatory research.

Furthermore, due to the sequestration budget reductions, FDA has reduced staff training, impairing the Agency's ability to remain current on the most recent scientific and regulatory advances. A major reduction in travel also means FDA cannot as readily interact with key stakeholders and regulatory partners. Additionally, the development of reports, guidances, rules, and *Federal Register* notices to implement FDASIA provisions has been delayed.

Any further reductions to FDA's resources in FY 2014 will exacerbate the challenges FDA faced as a result of the FY 2013 sequestration.

3. **How has sequestration affected product review times, if at all? Are certain products/review divisions/therapeutic areas more or less impacted than others?**

   How has sequestration, including of industry-paid user fees, impacted the Agency's ability to implement FDASIA in terms of the new responsibilities it is

required to undertake with respect to promoting innovation, stakeholder engagement, and drug supply chain integrity?

FDA did not have the additional resources needed to meet the new commitments made under PDUFA V that offered critical enhancements to communications with sponsors, new drug regulatory science, and more efficient and effective post-market safety oversight, beginning in FY 2013.

It is expected that all of the gains FDA has made in bringing PDUFA performance back to the 90 percent or greater goal performance are at risk, and FDA may no longer be able to meet critical performance goals for new drug review. This means potential delays in the availability of new drugs for patients and increased costs and adverse economic impacts on the U.S. pharmaceutical industry.

FDA's capacity to effectively launch the new user fee programs, GDUFA and BsUFA, has been reduced. These programs are designed to enable FDA to leverage user fee resources to provide many benefits to the public, including expediting the availability of high-quality, cost-effective generic drugs and biosimilars. FDA's ability to meet the performance goals negotiated with industry, including performance goals for expediting the review of generic drugs and biosimilars, is at risk. This may result in significantly delayed access to more affordable drug and biological products for patients.

FDA plans to meet key performance commitments negotiated under MDUFA III, such as improvements to premarket approval (PMA) goals and 510(k) goals. Sequestration made it challenging for FDA to meet MDUFA performance goals, but FDA minimized the impact of sequestration, where possible. FDA does not believe sequestration will impact MDUFA review times.

Any further reductions to FDA's resources in FY 2014 will exacerbate the challenges FDA faced as a result of the FY 2013 sequestration.

4. **It seems that the decision to sequester the PDUFA user fees violates the intent of the statute that the industry's user fees should only be used for the review of new medicines. Has the agency discussed any strategy to release the sequestered fees through the FY2014 fiscal process or otherwise?**

   Have you talked to either the House or Senate Appropriations Committees about finding a mechanism to release the fees? Has FDA requested that HHS or OMB release the fees? When and who took part in these discussions?

   Has FDA questioned OMB's analysis that PDUFA user fees are subject to sequester or any other use than for FDA's human drug review program? If so, when did FDA have these discussions and with whom?

FDA has discussed this issue within the Administration and with Congressional staff. We are pleased that the FY 2014 appropriation restores $124 million in budget authority

to FDA, lost due to the FY 2013 sequestration and rescission cuts. Section 747 of the FY 2014 appropriation also includes funding for the FY 2013 sequestered user fees.

5. **FDA continues to be unable to access approximately $83 million in sequestered user fees for FY2013. The loss of these fees has meant that the implementation of key aspects of FDASIA have been delayed including the hiring of any new scientific and medical personnel to advance crucial regulatory science priorities. Undoubtedly, this is bad for patients, bad for science and bad for public health. Given the gravity of the impact losing these fees has had on the agency's ability to fulfill its public health mission, shouldn't a mechanism to release them be among the Agency's top priorities for anomalies in any end of year fiscal package? Has the agency communicated with the Hill about such an anomaly? If so, to whom and when?**

FDA has discussed this issue within the Administration and with Congressional staff. We are pleased that the FY 2014 appropriation restores $124 million in budget authority to FDA, lost due to the FY 2013 sequestration and rescission cuts. Section 747 of the FY 2014 appropriation also includes funding for the FY 2013 sequestered user fees.

6. **Budget and Appropriations leaders have indicated that giving "flexibility" to agencies in how sequester cuts are implemented is a top priority for the end of year fiscal package. What kind of authority would FDA need for there to be a real impact on how effectively the agency is able to mitigate the impact of the sequester, including user fee programs? Have you communicated this to Budget and Appropriations negotiators by providing them with language or engaging in any conversations at all?**

FDA has discussed this issue within the Administration and with Congressional staff. We are pleased that the FY 2014 appropriation restores $124 million in budget authority to FDA, lost due to the FY 2013 sequestration and rescission cuts. Section 747 of the FY 2014 appropriation also includes funding for the FY 2013 sequestered user fees.

The Honorable Gus Bilirakis

1. **I am concerned about FDA's actions regarding combination products. Given that there are numerous products classified as devices that have some chemical action within or on the body of man, would you agree that the draft guidance, "Classification of Products as Drugs and Devices & Additional Product Classification Issues," reflects a substantial policy change by requiring a product to be classified as a drug if any of its intended purposed are achieved through a chemical action within or on the body of a man?**

As you note, FDA issued the Draft Guidance on Classification of Products as Drugs and Devices & Additional Product Classification Issues[31] (Classification Guidance) and

[31] Available at *http://www.fda.gov/RegulatoryInformation/Guidances/ucm258946.htm.*

related Draft Guidance on Interpretation of the Term "Chemical Action" in the Definition of Device under Section 201(h) of the FD&C Act[32] (Chemical Action Guidance) in 2011. These draft guidance documents concern classification of products as drugs and devices. The Agency is currently evaluating these draft guidance documents in light of the U.S. District Court for the District of Columbia's September 2012 opinion in *Prevor v. Food and Drug Admin. (Prevor I)*, 895 F. Supp. 2d 90 (D.D.C. 2012), and opinion in *Prevor v. Food and Drug Admin. (Prevor II)*, Case No. 1:13-cv-01177-RMC (D.D.C. Sept. 9, 2014).

2. **Would you agree that similar products should be regulated in the same manner and that the substantial policy change could have an impact on new products being regulated similarly to products on the market prior to issuance of the draft guidance?**

FDA strives to regulate similar products in a similar manner. FDA classifies products in accordance with the statutory definitions established by Congress. Differences in product composition or intended uses, or both, can affect product classification. Due to such factors, products that appear to be similar may, in fact, not be similar and, thus, have different classifications.

3. **The plain language of the Act indicates that a device may have more than one primary purpose. The 2011 FDA draft guidance appears to arbitrarily depart from this plain language. What is the rationale for doing so?**

We agree that a device may have more than one primary intended purpose.

4. **This draft guidance has not been finalized but appears to have been implemented by FDA. Would you agree that a draft guidance document should not be implemented until finalized?**

FDA follows its regulations at 21 CFR 10.115 in developing guidance documents. Accordingly, FDA agrees that when the Agency issues a draft guidance document setting forth "changes in interpretation or policy that are of more than a minor nature," FDA should not implement that guidance document until it is finalized (see 21 CFR 10.115(c)(1). However, FDA must implement its statutes and regulations, regardless of whether it chooses to issue guidance in an effort to provide greater detail and transparency to industry and other stakeholders.

The Agency is currently evaluating its "Classification" and "Chemical Action" draft guidance documents, in light of the U.S. District Court for the District of Columbia's rulings in *Prevor I* and *Prevor II*. FDA follows its regulations at 21 CFR 10.115 in developing guidance documents.

5. **The FDA recently applied its revised interpretation of the Federal Food, Drug and Cosmetic Act in the 2011 draft guidance to classify a portable body shower**

[32] Available at *http://www.fda.gov/RegulatoryInformation/Guidances/ucm259059.htm.*

as a drug rather than a medical device. The U. S. District Court for the District of Columbia found that the FDA designation of the product as a drug was based on a "doubly grandiose" interpretation of the phrase "primary intended purpose." When and how will FDA revise the 2011 draft guidance to reflect the ruling?

The Agency is currently evaluating its "Classification" and "Chemical Action" draft guidance documents in light of the U.S. District Court for the District of Columbia's rulings in *Prevor I* and *Prevor II*. We note that the product to which you refer—Diphoterine Skin Wash—is not a "portable body shower." It is comprised of a pressurized canister that delivers a diphoterine solution onto the skin as an aerosolized mist. Its primary intended purpose is to help prevent or minimize accidental chemical burn injuries. The diphoterine solution is expected to react with harmful chemicals to neutralize them, draw chemicals from the interior to the exterior of the skin, and displace chemicals from the body. The device canister aids in delivery of the diphoterine solution by allowing its ready delivery onto the skin. FDA classified the product as a combination product, consisting of a drug constituent part (the diphoterine solution) and a device constituent part (the aerosol spray canister), with a drug primary mode of action to that the Center for Drug Evaluation and Research (CDER) was designated as the lead Center for premarket review and regulation of the product. The Agency is currently evaluating its classification of Prevor's product in light of the U.S. District Court for the District of Columbia's ruling *Prevor II*.

6. **In response to the ruling, FDA created a new "meaningful contribution" standard for determining if a product is a device. Please explain how FDA developed its "meaningful contribution" test, and what criteria FDA will apply in determining whether that test is met. How is it that FDA can reinterpret statute at will against court directions?**

The Agency is currently evaluating its interpretation of the relevant statutory language in light of the U.S. District Court for the District of Columbia's rulings in *Prevor I* and *Prevor II*.

7. **Would you agree that requiring companies to comply with U.S. drug regulations, when they are required to comply with medical devices regulations in all other countries for the identical product, places an unreasonable burden on the companies and could prevent introduction of important products to U.S. patients? That is apparently the case with the portable body shower.**

Some products that are regulated as drugs in the United States are regulated as devices in other countries and vice versa. FDA classifies products in accordance with the statutory definitions in force in the United States. We seek to implement our regulatory programs for drugs and devices in a manner that is consistent with U.S. law and our mission to protect the public health, without imposing undue burden. We have developed regulatory programs to facilitate the development and availability of important products for U.S. patients. These include drug and device review programs. We remain committed to

pursuing efforts with foreign counterparts to pursue regulatory coherence to minimize regulatory burden consistent with U.S. law and the promotion and protection of the public health.

During the hearing, Members asked you to provide additional information for the record and you indicated that you would provide that information. For your convenience, descriptions of the requested information based on the relevant excerpts from the hearing transcript regarding these requests are provided below.

The Honorable Joseph R. Pitts

1. **Under MDUFA III, industry and the FDA agreed to have an independent two-phase assessment and program evaluation to objectively assess the FDA's premarket review process. Would you please submit a compiled list of recommendations in its entirety to the Committee upon its completion?**

The final written report on BAH's high-priority recommendations for the MDUFA III Independent Assessment was delivered to FDA on December 6, 2013, and was posted on the Agency's public website on December 11, 2013. A copy of the report is available at *http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/Overview/MDUFAIII/UCM378202.pdf*.

The Honorable Lois Capps

1. **Will you please give me an update on where the agency is with Sentinel?**

Section 615 of FDASIA explicitly requires expansion of active post-market risk identification and analysis to include and apply to medical devices.

In September 2012, FDA released an initial report, "Strengthening Our National System for Medical Device Postmarket Surveillance," which provided an overview of FDA's medical device post-market authorities and the current U.S. medical device post-market surveillance system, and also proposed four specific actions to strengthen the medical device post-market surveillance system in the United States. These actions include the expansion of the active surveillance approach of Sentinel to medical devices. This report can be found at *http://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDRH/CDRHReports/UCM301924.pdf*. Following release of the report, FDA held a series of public meetings in September 2012, including one focused on Sentinel, and accepted comments via its website to garner stakeholder feedback.

The update to the report, issued in April 2013, incorporates the public input that FDA received and details the concrete steps that the Agency will complete to more efficiently

collect better and timely data, helping to identify safety issues more quickly. This update to the report can be found at *http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDRH/CDRHReports/ucm301912.htm*.

Two implementation action items that the Agency identified include the establishment of a (1) National Medical Device Postmarket Surveillance Planning Board (Planning Board) and (2) National Medical Device Registry Task Force (Registry Task Force).

To facilitate establishment of the Planning Board, FDA's Center for Devices and Radiological Health (CDRH) awarded a cooperative agreement to the Brookings Institution to convene and manage the Planning Board.

To facilitate establishment of the Registry Task Force, CDRH awarded a cooperative agreement to Duke University to leverage the existing Medical Device Epidemiology Network (MDEpiNet) Public-Private Partnership via the MDEpiNet Partnership Coordinating Center at Duke University. The calls for nominations for the Planning Board and the Registry Task Force were issued on December 18, 2013, and nominations were accepted until January 17, 2014.

In addition, CDRH issued two five-year announcements for cooperative agreements to support building of public-private partnerships to implement the National Medical Device Postmarket Surveillance Plan through development of new data sources, epidemiology infrastructure, analysis methodologies, analysis tools, and registries. CDRH awarded cooperative agreements in September 2013, which will support the initial stages of development of the Registry Task Force through the MDEpiNet partnership coordination center at Duke University and will support convening the Planning Board through the Brookings Institution. Awards were also made to: (1) the Lahey Clinic for examination of Data Extraction and Longitudinal Trend Analysis (DELTA) software as a prospective active surveillance tool, (2) the University of Washington to develop the Dynamic Automated External Defibrillator (AED) Registry, and (3) Weill Cornell Medical College to develop an international consortium of cardiovascular registries. Each of these efforts involves substantial contribution from a broad array of external stakeholders in both the public and private sectors working toward common public health goals.

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